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NEWS 16	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 17	Oct 22	Over 1 million reactions added to CASREACT
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NEWS 19	Oct 29	AAASD no longer available
NEWS 20	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS 21	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
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NEWS 23	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
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FILE 'CAPLUS' ENTERED AT 12:12:39 ON 05 DEC 2001

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L1 25 ADMINSTERING

=> s l1 and bee venom

L2 0 L1 AND BEE VENOM

=> s bee venom

L3 7626 BEE VENOM

=> s l3 and anesthetic

L4 14 L3 AND ANESTHETIC

=> dup remove l4

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L5 10 DUP REMOVE L4 (4 DUPLICATES REMOVED)

=> d l5 1-10 cbib abs

L5 ANSWER 1 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
2001217360 EMBASE Skin testing in the evaluation of hymenoptera allergy and drug allergy. Graham D.M.; McPherson H.; Lieberman P.. Dr. P. Lieberman, 300 Walnut Bend Road South, Cordova, TN 38018, United States. Immunology and Allergy Clinics of North America 21/2 (301-320) 2001.
Refs: 88.
ISSN: 0889-8561. CODEN: INCAEP. Pub. Country: United States. Language: English. Summary Language: English.
AB This article discusses allergic reactions to insect stings and adverse drug reactions. Insect sting anaphylaxis is a relatively common problem estimated to affect at least 0.4% of the population and is responsible for

at least 50 deaths per year in the United States. The natural history, causative agents, venom constituents, and diagnosis of insect stings are presented, as well as venom selection. Reactions to penicillin, cephalosporins, insulin, local **anesthetics**, and protamine are also discussed.

L5 ANSWER 2 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
2001312712 EMBASE Improving clinical allergy services in the UK. Holgate S.T.. Dr. S.T. Holgate, Department of Immunopharmacology, School of Medicine, University of Southampton, Southampton, United Kingdom. Asthma Journal 6/3 (118-119) 2001.
ISSN: 1363-268X. CODEN: ASJOFG. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB As the prevalence of allergic disease increases, Stephen Holgate calls for action tto develop the UK's woefully inadequate specialist allergy services.

L5 ANSWER 3 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1
1998031664 EMBASE Radioprotection: Mechanisms and radioprotective agents including honeybee venom. Varanda E.A.; Tavares D.C.. E.A. Varanda, Departamento de Ciencias Biologicas, Faculdade Ciencias Farm. Araraquara, Rodovia Araraquara-Jau Km 01, CEP 14.801-902 Araraquara, Sao Paulo, Brazil. Journal of Venomous Animals and Toxins 4/1 (5-21) 1998.
Refs: 76.
ISSN: 0104-7930. CODEN: JVTOFG. Pub. Country: Brazil. Language: English. Summary Language: English.
AB Since 1949, a great deal of research has been carried out on the radioprotective action of chemical substances. These substances have shown to reduce mortality when administered to animals prior to exposure to a lethal dose of radiation. This fact is of considerable importance since it permits reduction of radiation-induced damage and provides prophylactic treatment for the damaging effects produced by radiotherapy. The following radioprotection mechanisms were proposed: free radical scavenger, repair by hydrogen donation to target molecules, formation of mixed disulfides, delay of cellular division and induction of hypoxia in the tissues. Radioprotective agents have been divided into four major groups: the thiol compounds, other sulfur compounds, pharmacological agents (**anesthetic** drugs, analgesics, tranquilizers, etc.) and other radioprotective agents (WR-1065, WR-2721, vitamins C and E, glutathione, etc.). Several studies revealed the radioprotective action of Apis mellifera honeybee venom as well as that of its components mellitin and histamine. Radioprotective activity of **bee venom** involves mainly the stimulation of the hematopoietic system. In addition, release of histamine and reduction in oxygen tension also contribute to the radioprotective action of **bee venom**.

L5 ANSWER 4 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
95127532 EMBASE Document No.: 1995127532. White paper: Chemical sensitivity: History and phenomenology. Miller C.S.. Dept. of Family Practice, Environmental/Occupational Medicine, Texas Univ. Health Science Center,San Antonio, TX 78284, United States. Toxicology and Industrial Health 10/4-5 (253-276) 1994.
ISSN: 0748-2337. CODEN: TIHEEC. Pub. Country: United States. Language: English. Summary Language: English.
AB Nearly everyone has heard something about chemical sensitivity, either from personal experience with someone who has the condition or from the media. The television series Northern Exposure recently featured a

chemically sensitive attorney who lived in a geodesic dome in Alaska, and L.A. Law depicted the struggles of a Persian Gulf veteran with chemical sensitivities who lost his case against the Veterans Administration, but may appeal later in the season. Television news programs and the printed media have showcased patients living spartan existences in remote areas or in aluminum foil-lined rooms. Our views of the illness no doubt are colored by our own personal experiences of it. While some discount or make jokes about chemical sensitivity or these patients, physicians who have seen a number of them are discovering that many appear to be credible individuals with prior good work records who say they became ill following an identifiable exposure to chemicals.

L5 ANSWER 5 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
92294512 EMBASE Document No.: 1992294512. Overview of toxins and drugs as tools to study excitable membrane ion channels: I. Voltage-activated channels. Narahashi T.; Herman M.D.. Department of Pharmacology, Northwestern Univ. Medical School,Chicago, IL 60611, United States. Methods in Enzymology 207/- (620-643) 1992.
ISSN: 0076-6879. CODEN: MENZAU. Pub. Country: United States. Language: English.

L5 ANSWER 6 OF 10 MEDLINE
89352470 Document Number: 89352470. PubMed ID: 2765482. Interaction of melittin with phosphatidylcholine membranes. Binding isotherm and lipid head-group conformation. Kuchinka E; Seelig J. (Department of Biophysical Chemistry, Biocenter of the University of Basel, Switzerland.)
BIOCHEMISTRY, (1989 May 16) 28 (10) 4216-21. Journal code: A0G; 0370623.
ISSN: 0006-2960. Pub. country: United States. Language: English.
AB The binding of melittin to nonsonicated bilayer membranes composed of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine was studied with an ultracentrifugation assay and with 2H and 31P nuclear magnetic resonance. Melittin binding could best be described by a partition equilibrium with Kp = (2.1 +/- 0.2) X 10(3) M-1, measuring the binding isotherm in the concentration range of 0-100 microM melittin and taking into account electrostatic effects by means of the Gouy-Chapman theory. This partition coefficient is smaller than that deduced for small sonicated vesicles and attests to the tighter lipid packing in the nonsonicated bilayers. Deuterium magnetic resonance revealed a conformational change of the phosphocholine head group upon melittin binding. The quadrupole splittings of the alpha and beta segments of the choline head group varied linearly with the amount of bound melittin but in opposite directions; i.e., the alpha splitting decreased, and the beta splitting increased. This conformational change is not specific to melittin but is a response of the phosphocholine head group to positive membrane surface charges in general. Quantitatively, melittin is one of the most efficient head-group modulators, the efficiency per unit charge comparable to that of charged local **anesthetics** or hydrophobic ions.

L5 ANSWER 7 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
85114308 EMBASE Document No.: 1985114308. Anaphylactoid reactions during anaesthesia. Seven years' experience of intradermal testing. Galletly D.C.; Treuren B.C.. Department of Anaesthesia, Wellington Hospital, Wellington, New Zealand. Anaesthesia 40/4 (329-333) 1985.
CODEN: ANASAB. Pub. Country: United Kingdom. Language: English.
AB Sixty one patients who had suffered intra-operative anaphylactoid reactions were studied. Intradermal testing identified the causative agent in 84% of cases and, in 75% of these, muscle relaxants were responsible.

Predisposing factors in patients sensitive to muscle relaxants were: female sex, previous allergy and atopy. The incidence of previous exposure was considerably higher than that reported in the literature. Pancuronium is suggested to be the least likely currently available agent to provoke a major anaphylactoid reaction.

L5 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2001 ACS
1984:588491 Document No. 101:188491 Neuromuscular and hormonal control of post-eclosion processes in flies. Fraenkel, Gottfried; Su, Jack; Zdarek, Jan (Dep. Entomol., Univ. Illinois, Urbana, IL, 61801, USA). Arch. Insect Biochem. Physiol., 1(4), 345-66 (English) 1984. CODEN: AIBPEA. ISSN: 0739-4462.
AB Flies (exemplified by Sarcophaga bullata) expand after eclosion from the puparium by processes of pulsing (slow rhythmical abdominal contractions) and pumping of air (fast rhythmical contractions of the cibarial pump). Pulsing and pumping are inhibited if a newly eclosed fly is kept in an enclosed space (sand, a glass tube, an empty puparium). This inhibition no longer applies if such flies are injected with either hemolymph from flies 10-15 min old or cAMP, or are confined at the age of 10 min. This suggests a hormonal control of pulsing and pumping. Pumping alone, without pulsing, occurs in flies treated with certain paralyzing agents like ether, tetrodotoxin, **bee venom**, or FlyNap (**anesthetic**), or have the connectives in the neck cut or interrupted by cauterization. Application of FlyNap or neck cauterization leads to excessive pumping which results in bloating. Expansion by bloating is confined to the soft membranes, leaving sclerites and wings largely unexpanded. The function of pulsing is probably that of plasticizing and stretching the cuticle to make it respond to increased steady pressure by air-pumping. Flies ligated at the proboscis show almost regular pulsing and pumping, but without intake of air, and consequently no expansion. Cuticle (sclerites) and wings, however, become plasticized. Some plasticization occurs even in the absence, or redn., of pulsing (in a neck-cauterized fly), brought about by a hormonal process. Eclosion from the puparium is also initiated by a hormonal action. Thus, the following processes during fly emergence are controlled by hormones: eclosion proper, pulsing, pumping, plasticization, and tanning. These hormones are sep. entities, with the possible exception of the pulsing/pumping hormone(s).

L5 ANSWER 9 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
83058327 EMBASE Document No.: 1983058327. [Anaphylactic shock. Results of a national study of 1047 cases]. LE CHOC ANAPHYLACTIQUE. RESULTATS D'UNE ENQUETE NATIONALE PORTANT SUR 1047 CAS. Mantz J.M.; Pauli G.; Meyer P.; et al.. Serv. Reanim. Med., Hosp. Civ., 67091 Strasbourg, France. Revue de Medecine Interne 3/4 (331-338) 1982.
CODEN: RMEIDE. Pub. Country: France. Language: French. Summary Language: English.
AB Results of a multicentric French study of 1047 cases of anaphylactic shock seen during the past 6 years are reported. **Anesthetics** and curarizing drugs, hymenoptera venoms, analgesics, iodine-containing contrast products and antibiotics are responsible for 75% of the cases. Hyperacute forms of anaphylactic shock, clinically manifested by cardiovascular signs, are represented by one third of the cases in the series. The remaining two thirds concern subacute cases dominated by cutaneous, respiratory, digestive or neurological signs. In half the cases, anaphylactic shock developed less than 5 minutes after contact with

the allergen. Contrary to widespread opinion, there exists a correlation between the severity of the clinical state and certain laboratory parameters (leukopenia, lowering of serum complement). Diverse therapeutic measures were employed; corticotherapy was applied in 90% of the cases, adrenaline in only 16%. The authors deplore the loss of 32 of the 1047 patients (3%).

L5 ANSWER 10 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 2
78228132 EMBASE Document No.: 1978228132. Induction of ATP depletion, intramembrane particle aggregation and exposure of membrane phospholipids in chicken erythrocytes by local **anesthetics** and tranquilizers.
Gazitt Y.; Loyter A.; Ohad I.. Dept. Biol. Chem., Hebrew Univ. Jerusalem, Israel. Biochimica et Biophysica Acta 471/3 (361-371) 1977.
CODEN: BBACAQ. Pub. Country: Netherlands. Language: English.
AB Incubation of chicken erythrocytes with 1 mM tetracaine, 10 mM lidocaine and 0.24-0.48 mM chlorpromazine significantly reduced the ATP content of the cells, while procaine even at concentrations as high as 10 mM had only a slight effect. When chlorpromazine was used, it was found that the final level of the ATP was dependent on the drug concentration, which at 0.48 mM depletes the cells to about 10% of the initial ATP content. The ATP depletion of chicken erythrocytes was accompanied by dephosphorylation of certain membrane proteins which were identified by acrylamide gel electrophoresis as an 180,000 dalton protein band and peptides with molecular weight of 60,000-100,000. Treatment of chicken and rat erythrocytes with 0.5 mM tetracaine and 1 mM lidocaine or with 0.48 mM chlorpromazine induced significant aggregation of intramembrane particles as revealed by the freeze-etching technique. Procaine (10 mM) had no effect. Incubation of chicken erythrocytes with the above-mentioned drugs induced also exposre of the masked membrane phospholipids to the action of phospholipase-C (Bacillus cereus) and to phospholipase A2 (**bee venom**). Negligible amounts of phospholipids were hydrolyzed in the untreated cells, while about 40% of the membrane phosphatidylethanolamine and 50% of the phosphatidylcholine were hydrolyzed by phospholipase A2 in chicken erythrocytes treated with 0.48 mM chlorpromazine. Treatment of chicken and rat erythrocytes with 0.48 mM chlorpromazine resulted also in an increase in the amount of the phospholipid fraction which could be extracted by dry ether. About 41% and 60% of phospholipids were extracted from chlorpromazine-treated chicken and rat erythrocytes, respectively, as compared to 25% and 35% of phospholipids extracted from the same untreated cells.

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 12:12:39 ON 05 DEC 2001

L1	25	S ADMINSTERING
L2	0	S L1 AND BEE VENOM
L3	7626	S BEE VENOM
L4	14	S L3 AND ANESTHETIC
L5	10	DUP REMOVE L4 (4 DUPLICATES REMOVED)

=> s l3 and coadministration

L6 2 L3 AND COADMINISTRATION

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L7 2 DUP REMOVE L6 (0 DUPLICATES REMOVED)

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L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS
1993:167348 Document No. 118:167348 Ricin enhances IgE responses by inhibiting a subpopulation of early-activated IgE regulatory CD8+ T cells.
Diaz-Sanchez, D.; Lee, T. H.; Kemeny, D. M. (United Med. Sch., Guy's Hosp., London, UK). Immunology, 78(2), 226-36 (English) 1993. CODEN: IMMUAM. ISSN: 0019-2805.
AB Ricin, a toxic lectin from castor beans greatly enhances IgE responses to **bee venom** phospholipase A2 (PLA2) in high and low IgE responder strains of rat. The increase in IgE is accompanied by a 60% redn. in the no. of CD8+ but not CD4+ T cells in the spleen. Optimal enhancement of IgE by ricin occurs when it is given at the same time as the antigen or 24 h later, suggesting that it acts on cells which were activated as a consequence of immunization. Radioligand-binding studies with 125I ricin were used to compare the no. of ricin binding sites on CD4+ and CD8+ T cells. No difference was seen in either the affinity or the no. of receptors for ricin on the CD4+ and CD8+ T cells of unimmunized rats. In contrast, CD8+ T cells taken from rats which had been immunized with 10 .mu.g of PLA2 24 h earlier demonstrated considerably more ricin receptors (3.9 .times. 107 binding sites/cell) than CD4+ T cells (3.19 .times. 106 binding sites/cell). However the affinity of the receptors for ricin was unchanged. Cytofluorog. anal. with fluorescein isothiocyanate (FITC)-labeled ricin confirmed these observations and indicated that increased ricin binding occurred on a subpopulation of CD8+ T cells. The effect of CD8+ T cells on IgE regulation was investigated by adoptive transfer. 1 .times. 108 Highly purified (>98%) splenic CD8+ T cells collected from Brown Norway rats 3 days after immunization with 10 .mu.g of PLA2 were adoptively transferred to naive, syngeneic recipients. The IgE antibody response to PLA2+Al(OH)3 seen in these animals was reduced by 91%. Adoptive transfer of CD4+ T cells from the same donor animals did not induce suppression and nor did adoptive transfer of CD8+ T cells from animals given both ricin and PLA2. However, when recipients of CD8+ T cells taken from rats immunized with PLA2 were immunized with a different antigen [ovalbumin (OVA)] and Al(OH)3, the IgE antibody response was also suppressed, although to a lesser extent (66%). These results show that **coadministration** of ricin and PLA2 depletes a subpopulation of ricin-sensitive, early activated CD8+ T cells and that these CD8+ T cells are potent suppressors of the primary IgE response.

L7 ANSWER 2 OF 2 SCISEARCH COPYRIGHT 2001 ISI (R)
91:123024 The Genuine Article (R) Number: EZ247. GENERATION OF A LONG-LIVED IGE RESPONSE IN HIGH AND LOW RESPONDER STRAINS OF RAT BY **COADMINISTRATION** OF RICIN AND ANTIGEN. DIAZSANCHEZ D; KEMENY D M (Reprint). GUYS & ST THOMAS HOSP, UNITED MED & DENT SCH, DEPT ALLERGY & ALLIED RESP DIS, DIV MED, LONDON SE1 9RT, ENGLAND; ST THOMAS HOSP, UNITED MED & DENT SCH, LONDON SE1 7EH, ENGLAND. IMMUNOLOGY (1991) Vol. 72, No. 2, pp. 297-303. Pub. country: ENGLAND. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Certain strains of rats infested with the nematode parasite Nippostrongulus brasiliensis mount vigorous, persistent immunoglobulin E (IgE) responses. In the absence of parasites, adjuvants such as Bordatella pertussis or Al(OH)3 are needed to produce IgE responses to soluble antigens. These are short-lived, even in high IgE responder strains. In this study we have produced long-lived IgE responses in both low (Wistar) and high (Brown Norway) IgE responder strains of rats by repeated injections of ricin, a toxic lectin from castor beans, and phospholipase A2 (PLA2), a **bee venom** protein. Total IgE levels rose from 30 +/- 20 ng/ml to 39,000 +/- 7500 ng/ml in the Wistar rats compared with an increase from 120 +/- 100 ng/ml to 47,000 +/- 8000 ng/ml in the Brown Norway rats. An even greater (10(4)-fold) increase was seen in PLA2-specific IgE antibody levels. Total and PLA2-specific IgE started to fall 6 weeks after treatment was stopped in the Wistar and after 12 weeks in the Brown Norway rats. The duration of the response was 204 and 248 days, respectively. The IgE-enhancing properties of ricin were compared in low, mid (Hooded Lister) and high IgE responder rats. Total IgE and PLA2-specific IgE but not IgG antibody (Ab) responses were enhanced in all animals given ricin and PLA2 but not in animals given ricin or PLA2 alone. The increase was greater in Wistar rats (48-fold) than in Brown Norway rats (eightfold) and by Day 24 the levels of both total and PLA2-specific IgE in the three different strains were indistinguishable. PLA2-specific IgE antibody-secreting cells were detected in the spleen at a frequency of 1:5000. These results show: (i) that repeated immunization of rats with antigen and ricin produce a very large IgE response which was long-lived; (ii) that this response was indistinguishable in different IgE responder strains of rat; and (iii) that the IgE response declines earlier in low IgE responder strains of rats.

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     05 DEC 2001
L1           25 S ADMINSTERING
L2            0 S L1 AND BEE VENOM
L3         7626 S BEE VENOM
L4           14 S L3 AND ANESTHETIC
L5           10 DUP REMOVE L4 (4 DUPLICATES REMOVED)
L6            2 S L3 AND COADMINISTRATION
L7            2 DUP REMOVE L6 (0 DUPLICATES REMOVED)

=> s l3 and rheumatoid arthritis

L8           43 L3 AND RHEUMATOID ARTHRITIS

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L9           25 DUP REMOVE L8 (18 DUPLICATES REMOVED)

=> d l9 1-25 cbib abs


L9   ANSWER 1 OF 25     MEDLINE                          DUPLICATE 1
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2001305459 Document Number: 21157700. PubMed ID: 11207399. **Bee venom** injection into an acupuncture point reduces arthritis associated edema and nociceptive responses. Kwon Y B; Lee J D; Lee H J; Han H J; Mar W C; Kang S K; Beitz A J; Lee J H. (Department of Veterinary Physiology, College of Veterinary Medicine and School of Agricultural Biotechnology, Seoul National University, Suwon 441-744, South Korea.) PAIN, (2001 Feb 15) 90 (3) 271-80. Journal code: OPF; 7508686. ISSN: 0304-3959. Pub. country: Netherlands. Language: English.

AB **Bee venom** (BV) has traditionally been used in Oriental medicine to relieve pain and to treat inflammatory diseases such as **rheumatoid arthritis** (RA). While several investigators have evaluated the anti-inflammatory effect of BV treatment, the anti-nociceptive effect of BV treatment on inflammatory pain has not been examined. Previous studies in experimental animals suggest that the therapeutic effect of BV on arthritis is dependent on the site of administration. Because of this potential site specificity, the present study was designed to evaluate the anti-nociceptive effect of BV injections into a specific acupoint (Zusanli) compared to a non-acupoint in an animal model of chronic arthritis. Subcutaneous BV treatment (1 mg/kg per day) was found to dramatically inhibit paw edema caused by Freund's adjuvant injection. Furthermore, BV therapy significantly reduced arthritis-induced nociceptive behaviors (i.e. the nociceptive scores for mechanical hyperalgesia and thermal hyperalgesia). These anti-nociceptive/anti-inflammatory effects of BV were observed from 12 days through 21 days post-BV treatment. In addition, BV treatment significantly suppressed adjuvant-induced Fos expression in the lumbar spinal cord at 3 weeks post-adjuvant injection. Finally, injection of BV into the Zusanli acupoint resulted in a significantly greater analgesic effect on arthritic pain as compared to BV injection in to a more distant non-acupoint. The present study demonstrates that BV injection into the Zusanli acupoint has both anti-inflammatory and anti-nociceptive effects on Freund's adjuvant-induced arthritis in rats. These findings raise the possibility that BV acupuncture may be a promising alternative medicine therapy for the long-term treatment of **rheumatoid arthritis**.

L9 ANSWER 2 OF 25 MEDLINE DUPLICATE 2

2001494227 Document Number: 21202124. PubMed ID: 11307924. **Bee venom** pretreatment has both an antinociceptive and anti-inflammatory effect on carrageenan-induced inflammation. Lee J H; Kwon Y B; Han H J; Mar W C; Lee H J; Yang I S; Beitz A J; Kang S K. (Department of Veterinary Physiology, College of Veterinary Medicine, Seoul National University, Suwon, South Korea.) JOURNAL OF VETERINARY MEDICAL SCIENCE, (2001 Mar) 63 (3) 251-9. Journal code: A27; 9105360. ISSN: 0916-7250. Pub. country: Japan. Language: English.

AB Although the injection of **bee venom** (BV) has been reported to evoke tonic pain and hyperalgesia, there is conflicting evidence in the literature indicating that BV can also exert an anti-inflammatory and antinociceptive effects on inflammation. In this regard, BV has been traditionally used in Oriental medicine to relieve pain and to treat chronic inflammatory diseases such as **rheumatoid arthritis**. The present study was designed to test the hypothesis that BV induces acute nociception under normal conditions, but that it can serve as a potent anti-inflammatory and antinociceptive agent in a localized inflammatory state. The experiments were designed to evaluate the effect of BV pretreatment on carrageenan (CR)-induced acute paw edema and thermal hyperalgesia. In addition, spinal cord Fos expression induced by peripheral inflammation was quantitatively analyzed. In normal animals subcutaneous BV injection into the hindlimb was found to slightly increase Fos expression in the spinal cord without producing detectable nociceptive

behaviors or hyperalgesia. In contrast pretreatment with BV (0.8 mg/kg) 30
min prior to CR injection suppressed both the paw edema and thermal hyperalgesia evoked by CR. In addition, there was a positive correlation between the percent change in paw volume and the expression of Fos positive neurons in the spinal cord. These results indicate that BV pretreatment has both antinociceptive and anti-inflammatory effects in CR-induced inflammatory pain. These data also suggest that BV administration may be useful in the treatment of the pain and edema associated with chronic inflammatory diseases.

L9 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2001 ACS
2000:191197 Document No. 132:232740 Protein and cDNA sequences of honey **bee venom** protein PX3.101, and uses thereof in the treatment of various diseases. Cui, Xiangmin; Lu, Yuefeng (Pan Pacific Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2000015774 A1 20000323, 80
pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US21077 19990913. PRIORITY: US 1998-100172 19980914.
AB The invention provides protein and cDNA sequences of a novel protein, PX3.101, which can be isolated from honey **bee venom**. The invention also provides pharmaceutical compns. based upon PX3.101 polypeptide and methods for using same in the treatment of various diseases, including various inflammatory diseases such as **rheumatoid arthritis**. The invention further relates to the treatment of diseases assocd. with chemokine (esp. IL-8) imbalances, wherein PX3.101 inhibits the binding of a chemokine with its receptor.

L9 ANSWER 4 OF 25 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:910556 The Genuine Article (R) Number: 377LA. Secreted phospholipase A(2) induces vascular endothelial cell migration. Rizzo M T (Reprint); Nguyen E; AldoBenson M; Lambeau G. CLARIAN HLTH, METHODIST RES INST, SIGNAL TRANSDUCT LAB, 1701 N SENATE BLVD, RM WG 30, INDIANAPOLIS, IN 46201
(Reprint); CLARIAN HLTH, ARTHRIT CARE CTR, INDIANAPOLIS, IN 46201; CNRS, INST PHARMACOL MOL & CELLULAIRE, UPR, F-06560 VALBONNE, FRANCE. BLOOD (1 DEC 2000) Vol. 96, No. 12, pp. 3809-3815. Publisher: AMER SOC HEMATOLOGY.
1900 M STREET. NW SUITE 200, WASHINGTON, DC 20036. ISSN: 0006-4971. Pub. country: USA; FRANCE. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Secreted phospholipase Ap (SPLA(2)) regulates a Variety of cellular functions. The present investigation was undertaken to elucidate the potential role of sPLA(2) in endothelial cell (EC) migration. Bovine aortic endothelial cells (BAECs) exposed to sPLA(2) placed in the lower compartment of a modified Boyden chamber displayed increased migration compared to cells exposed to vehicle. The effect of sPLA(2) on EC migration was time and dose dependent. Migration of BAECs was observed at 30 minutes, increased over 1 to 2 hours, and declined thereafter. At 2 hours of stimulation, sPLA2 (0.01-2 mu mol/L) induced 1.2- to 3-fold increased cell migration compared with media alone. Among the different sPLA(2)s tested, **bee venom**, Naja naja, and porcine and human pancreatic PLA(2)s all evoked a migratory response in ECs, Moreover, human synovial fluid, obtained from patients with arthritis and containing sPLA(2) activity, induced EC migration. Migration of ECs was significantly

reduced after exposure to a catalytic site mutant of pancreatic sPLA(2) with decreased lipolytic activity as compared to wild-type sPLA(2), Similarly, pretreatment of human synovial fluid with p-bromophenacyl bromide, an irreversible inhibitor of sPLA(2), markedly decreased the ability of human synovial fluid to stimulate EC migration. Moreover, migration of ECs was stimulated on exposure to hydrolytic products of sPLA(2) activity including arachidonic acid, lysophosphatidic acid, and lysophosphatidylcholine. These findings suggest that sPLA(2) plays a physiologic role in induction of EC migration. Moreover, the effects of sPLA(2) on EC migration are mediated, at least in part, by its catalytic activity. (C) 2000 by The American Society of Hematology.

L9 ANSWER 5 OF 25 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
2000204542 EMBASE Things do not get better by being left alone. The physician
and complementary medicine. Perlman A.I.. Dr. A.I. Perlman, Saint Barnabas
Health Care System, Saint Barnabas Ambulatory Care Ctr., Livingston, NJ 07039, United States. Aperlman@sbhcs.com. Journal of Rheumatology 27/6 (1332-1333) 2000.
Refs: 10.
ISSN: 0315-162X. CODEN: JRHUA. Pub. Country: Canada. Language: English.

L9 ANSWER 6 OF 25 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:693902 The Genuine Article (R) Number: 351VW. An 18.5 kDa protein from the amebocyte of Limulus polyphemus, homologous to the previously described amebocyte aggregation factor, expresses alternative phospholipase A(2) activity. MacPherson J C (Reprint); Jacobs R S. CLEVELAND CLIN FDN, DEPT CELL BIOL, 9500 EUCLID AVE, NC-10, CLEVELAND, OH 44195 (Reprint); UNIV CALIF SANTA BARBARA, DEPT ECOL EVOLUT & MARINE BIOL,
SANTA BARBARA, CA 93106. COMPARATIVE BIOCHEMISTRY AND PHYSIOLOGY B-BIOCHEMISTRY & MOLECULAR BIOLOGY (SEP 2000) Vol. 127, No. 1, pp. 31-44.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD. THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND. ISSN: 0305-0491. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A protein expressing phospholipase A(2) activity was purified from the granular amebocyte of the horseshoe crab, Limulus polyphemus by cation-exchange, size-exclusion chromatography and semi-preparative reverse-phase-high pressure liquid chromatography (RP-HPLC). The protein had an apparent mass of 17.7 kDa by SDS-polyacrylamide gel electrophoresis
(SDS-PAGE), but a more accurate estimate of 18.5 kDa was assigned by electrospray ionization-mass spectrometry (ESI MS). A partial sequence of this protein demonstrated total sequence homology with an 18.5 kDa protein
with cell aggregating properties from Limulus reported by Fujii et al. [J.
Biol. Chem. 267:22452,]. In these studies, the Limulus protein demonstrated a positive cross-reaction to polyclonal anti-human recombinant phospholipase A(2) (group II, 14 kDa). The protein did not display a significant loss of biological activity after boiling, but all enzymatic activity was lost after boiling in the presence of the reducing agent betamercaptoethanol (beta-mercaptoethanol). The Limulus protein was inhibited by manoalide, a covalent irreversible phospholipase A(2) inhibitor, in a dose-dependent fashion with 50% inhibition occurring at a concentration of 0.48 mu M. The Limulus protein displayed no activity in a
triglyceride lipase assay. These studies characterize an alternative phospholipase A(2) activity for the previously described 18.5 kDa protein from the L. polyphemus amebocyte. (C) 2000 Elsevier Science Inc. All rights reserved.

L9 ANSWER 7 OF 25 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
1999391245 EMBASE Venoms, copper, and zinc in the treatment of arthritis. Caldwell J.R.. Dr. J.R. Caldwell, Florida Arthritis and Allergy Inst., 311
North Clyde Marris Boulevard, Daytona Beach, FL 32114, United States. Rheumatic Disease Clinics of North America 25/4 (919-928) 1999.
Refs: 38.
ISSN: 0889-857X. CODEN: RDCAEK. Pub. Country: United States. Language: English. Summary Language: English.
AB This article discusses the use of venoms, copper, and zinc in the treatment of arthritis. The author examines the history and effectiveness of viper, bee, and ant venoms in order to determine whether these natural ingredients in anti-inflammatory medications help relieve a patient's symptoms. Copper and zinc studies may offer therapeutic benefits, but there is still no solid consensus on the potential role of these elements in treating arthritis.

L9 ANSWER 8 OF 25 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
1999206812 EMBASE Arthritis: New agents herald more effective symptom management. Simon L.S.. Dr. L.S. Simon, Graduate Medical Education, Beth Israel Deaconess Medical Center, Boston, MA, United States. Geriatrics 54/6 (37-44) 1999.
Refs: 15.
ISSN: 0016-867X. CODEN: GERIAZ. Pub. Country: United States. Language: English. Summary Language: English.
AB For physicians and patients alike, managing the symptoms of rheumatoid and
osteoarthritis is an ongoing challenge. Myriad therapies are available, virtually all provide only temporary relief and produce side effects that interrupt long-term use. New disease-modifying antirheumatic drugs, biologic response modifiers, and cyclooxygenase inhibitors offer the promise of more effective, longer lasting symptom management and, in some cases, reduced side effects. The population of older persons affected by arthritis continues to grow. Increased familiarity with these new treatments will aid primary care physicians in helping older patients better manage their arthritis during the next decade.

L9 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2001 ACS
1998:126370 Document No. 128:189186 Delivery of tolerogenic antigens via edible plants or plant-derived products. Welter, Lisa M. (Agrivax Incorporated, USA; Welter, Lisa M.). PCT Int. Appl. WO 9806861 A2 19980219, 47 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US13634 19970805. PRIORITY: US 1996-23973 19960815.
AB Autoantigens and allergens can be expressed in transgenic plants, and the plants, or products derived therefrom, used as foods or beverages to prevent or treat autoimmune diseases or allergic reactions. Thus, expression cassettes were constructed for the following transgenic plant systems: (1) human myelin basic protein expression in potato; (2) human type II collagen in corn; and (3) S-antigen and/or interphotoreceptor retinoid-binding protein IRBP in soybean and sunflower. Feeding transgenic potato contg. myelin basic protein was effective in mice with relapsing-remitting exptl. autoimmune encephalitis.

L9 ANSWER 10 OF 25 MEDLINE DUPLICATE 3
97446000 Document Number: 97446000. PubMed ID: 9299527. Melittin binds to
secretory phospholipase A2 and inhibits its enzymatic activity. Saini S S;
Peterson J W; Chopra A K. (Department of Microbiology and Immunology, University of Texas Medical Branch, Galveston, Texas 77555-1019, USA.) BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1997 Sep 18) 238 (2)

436-42. Journal code: 9Y8; 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Synthetic melittin inhibited the enzymatic activity of secretory phospholipase A2 (PLA2) from various sources, including bee and snake venoms, bovine pancreas, and synovial fluid from **rheumatoid arthritis** patients, irrespective of substrate (e.g., [14C]-phosphatidylcholine or phosphatidylethanolamine vesicles and [3H]-oleic acid-labeled E.coli). A Lineweaver-Burk analysis showed that melittin was a noncompetitive inhibitor of **bee venom** PLA2, causing a change in Vmax from 200 to 50 units/min/mg of protein. The Km remained unchanged (0.75 nmole). Melittin inhibited approximately 50% of purified **bee venom** PLA2 activity in a 30:1 molar ratio (melittin:enzyme). Because the enzyme kinetics indicated a PLA2-melittin interaction, a melittin-sepharose affinity column was used to purify a PLA2 from human serum. Further, an enzyme-linked assay was developed to quantitate PLA2 activity in biological fluids using avidin-peroxidase and ELISA plates coated with biotinylated melittin. These observations may have potential therapeutic significance, as well as provide a convenient basis for the isolation and quantitation of PLA2. Copyright 1997 Academic Press.

L9 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2001 ACS

1996:756546 Document No. 126:17804 Human antibodies derived from immunized xenomice. Kucherlapati, Raju; Jakobovits, Aya; Klapholz, Sue; Brenner, Daniel G.; Capon, Daniel J. (Cell Genesys, Inc., USA). PCT Int. Appl. WO 9634096 A1 19961031, 64 pp. DESIGNATED STATES: W: AU, CA, FI, HU, JP, KR, NO, NZ; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US5500 19950428.

AB Antibodies with fully human variable regions against a specific antigen can be prepd. by administering the antigen to a transgenic animal which has been modified to produce such antibodies in response to antigenic challenge, but whose endogenous loci have been disabled. Various subsequent manipulations can be performed to obtain either antibodies per se or analogs thereof.

L9 ANSWER 12 OF 25 MEDLINE DUPLICATE 4

95221909 Document Number: 95221909. PubMed ID: 7706741. Phospholipase A2-activating protein induces the synthesis of IL-1 and TNF in human monocytes. Bomalaski J S; Ford T; Hudson A P; Clark M A. (Medical College of Pennsylvania, Philadelphia 19129, USA.) JOURNAL OF IMMUNOLOGY, (1995 Apr 15) 154 (8) 4027-31. Journal code: IFB; 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Phospholipase A2-activating protein (PLAP) is an important mediator of eicosanoid generation. PLAP can also be found in high concentrations in synovial fluid from patients with **rheumatoid arthritis**, and injection of PLAP into animal joints results in an inflammatory, rheumatoid-like lesion. We have demonstrated previously that TNF-alpha and IL-1 beta stimulate formation of PLAP before phospholipase A2 (PLA2) enzyme activation and production of eicosanoids. To further explore the mechanisms found in the inflammatory response, we examined the ability of PLAP to stimulate release of TNF and IL-1 from human peripheral blood monocytes. TNF and IL-1 protein levels were measured by ELISA, and IL-1 and TNF mRNA were determined by Northern blotting. PLAP, PLAP peptide, and melittin, a **bee venom** PLA2 activator with homology with PLAP, all increased IL-1 and TNF production in a time- and dose-dependent manner. Heat-denatured PLAP and actin (an irrelevant protein) failed to exert this effect. PLAP stimulation of TNF and IL-1 could be enhanced with co-treatment of cells with free fatty acids, such

as arachidonic or linoleic acid, but it was not blocked completely by PLA2
inhibitors. These results demonstrate not only that synthesis of PLAP can be stimulated by cytokines, but also that PLAP may regulate cytokine synthesis and thus perpetuate an immune or inflammatory response.

L9 ANSWER 13 OF 25 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
92306856 EMBASE Document No.: 1992306856. Fatty acid amides: Scooting mode-based discovery of tight-binding competitive inhibitors of secreted phospholipases A2 [3]. Jain M.K.; Ghomashchi F.; Yu B.-Z.; Bayburt T.; Murphy D.; Houck D.; Brownell J.; Reid J.C.; Solowiej J.E.; Wong S.-M.; Mocek U.; Jarrell R.; Sasser M.; Gelb M.H.. Department of Chemistry/Biochemistry, University of Delaware,Newark, DE 19716, United States. Journal of Medicinal Chemistry 35/19 (3584-3586) 1992. ISSN: 0022-2623. CODEN: JMCMAR. Pub. Country: United States. Language: English.

L9 ANSWER 14 OF 25 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
90302592 EMBASE Document No.: 1990302592. **Bee venom** therapy for chronic pain. Klinghardt D.K.. 1468 Saint Francis Drive, Santa Fe, NM 87501, United States. Journal of Neurological and Orthopaedic Medicine and Surgery 11/3 (195-197) 1990. ISSN: 0890-6599. CODEN: JOMSEB. Pub. Country: United States. Language: English.

L9 ANSWER 15 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS
1989:329120 Document No.: BR37:31892. STIMULATION OF PHOSPHOLIPASE A-2 AND ARACHIDONIC ACID METABOLITE RELEASE BY HUMAN PHOSPHOLIPASE A-2 ACTIVATING PROTEIN PEPTIDES. BOMALASKI J S; FATTAL K A; CLARK M A. V.A. MED. CENT., MED. COLL. PA., UNIV. PA., PHILADELPHIA.. NATIONAL MEETING OF THE AMERICAN FEDERATION FOR CLINICAL RESEARCH, WASHINGTON, D.C., USA, APRIL 28-MAY 1, 1989. CLIN RES. (1989) 37 (2), 505A. CODEN: CLREAS. ISSN: 0009-9279. Language: English.

L9 ANSWER 16 OF 25 MEDLINE DUPLICATE 5
90022904 Document Number: 90022904. PubMed ID: 2552770.
Rheumatoid arthritis synovial fluid phospholipase A2 activating protein (PLAP) stimulates human neutrophil degranulation and superoxide ion production. Bomalaski J S; Baker D; Resurreccion N V; Clark M A. (V.A. Medical Center, Medical College of Pennsylvania, University of Pennsylvania, Philadelphia 19104.) AGENTS AND ACTIONS, (1989 Jun) 27 (3-4) 425-7. Journal code: 2XZ; 0213341. ISSN: 0065-4299. Pub. country: Switzerland. Language: English.
AB **Rheumatoid arthritis** is characterized by excessive eicosanoid production, and phospholipase enzymes are the rate limiting step in eicosanoid synthesis. We have shown previously that cells from patients with **rheumatoid arthritis** express enhanced phospholipase A2 enzyme activities. Recently, we have isolated a phospholipase A2 activating protein termed PLAP from rheumatoid synovial fluid. This novel human protein shares biochemical and antigenic similarities with melittin, a **bee venom** phospholipase activating protein. Because melittin has been shown to induce neutrophil degranulation and superoxide formation, and because exuberent release of lysosomal enzymes and superoxide have been implicated in the pathogenesis of **rheumatoid arthritis**, we examined the role of PLAP on inducing these neutrophil functions.

L9 ANSWER 17 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS
1989:429996 Document No.: BA88:88254. **BEE VENOM** THERAPY FOR ARTHRITIS. KIM C M. MONMOUTH PAIN INST. INC., RED BANK, N.J., U.S.A. 07701.. RHUMATOLOGIE, (1989) 41 (3), 67-72. CODEN: RHUMAY. Language:

English.
AB **Bee Venom** therapy for arthritis remains somewhat controversial. Unfortunately, there are very few controlled studies available to guide clinical practice. One Hundred and Eight patients with longstanding history of arthritis (RA or OA) who failed to respond to conventional medical treatment were used as subjects (Sept. 85 to Sept. 87). Participation was on a voluntary basis as denoted by informed consents from all subjects. All subjects were tested for possible allergic reaction before initial treatment. 0.1 ml. standard BV-10 was injected intradermally twice a week. The number of injections increased gradually each subsequent treatment until evaluation showed markedly improved or completely resolved. Pain was most common problem with subjects. Pain measure included the McGill Pain Questionnaire and Visual Analog Scales. Clinical evaluation included serial physical examinations and the thermographic findings. Each subject was followed 6 months to 2 years after finished treatment. Most of subjects, showed slight improvements after 3rd session and marked improvement average 12th treatment. Total 33,644 injections were given. No clinical complications or serious side effects were observed in any subjects who participated in the study. It was concluded the **bee venom** therapy is safe, effective and has no serious side effects, as long as a person is not allergic to **bee venom**. The preliminary results highly suggest that **bee venom** therapy is a new alternative approach for arthritis victims who failed to respond to the conventional medical treatments.

L9 ANSWER 18 OF 25 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 6
85014838 EMBASE Document No.: 1985014838. The effect of **bee venom** on plasma corticosterone levels. Dunn J.D.. Department of Anatomy, Oral Roberts University School of Medicine, Tulsa, OK 74171, United States. Neuroendocrinology Letters 6/5 (273-277) 1984. CODEN: NLETDU. Pub. Country: Germany. Language: English.

L9 ANSWER 19 OF 25 MEDLINE
80246539 Document Number: 80246539. PubMed ID: 6901677. [Drug therapy of **rheumatoid arthritis**]. Medikamentoznaia terapiia revmatoidnogo artrita. Rudyk B I. FELDSHER I AKUSHERKA, (1980) 45 (6) 8-10. Journal code: EVA; 16930040R. ISSN: 0014-9772. Pub. country: USSR. Language: Russian.

L9 ANSWER 20 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS
1976:67630 Document No.: BR12:67630. POSSIBLE THERAPEUTIC USE OF A PEPTIDE FROM **BEE VENOM**. BANKS B E C; RUMJANEK F D; SINCLAIR N M; VERNON C A. Bull. Inst. Pasteur (Paris), (1976) 74 (1), 137-144. CODEN: BIPAA8. ISSN: 0020-2452. Language: Unavailable.

L9 ANSWER 21 OF 25 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
75096141 EMBASE Document No.: 1975096141. The association of antinuclear antibodies with the chronic iridocyclitis of juvenile **rheumatoid arthritis** (Still's disease). Schaller J.G.; Johnson G.D.; Holborow E.J.; et al.. MRC Rheum. Unit, Canadian Red Cross Mem. Hosp., Maidenhead, United Kingdom. Arthritis and Rheumatism 17/4 (409-416) 1974. CODEN: ARHEAW. Language: English.
AB Positive tests for antinuclear antibodies (ANA) were found in 51 of 58 (88%) patients with chronic iridocyclitis and juvenile **rheumatoid arthritis** (Still's 26111w13=more. disease). Antinuclear antibodies were predominantly of the IgG class of immunoglobulins and were generally present in titers of 1:50 (6 ANA units) or more, They were unassociated with disease activity, severety or duration, age of patient at onset or testing, or sex. Neither other autoantibodies nor antibodies reactive with DNA or RNA were associated. In 8 patients tested early in disease, ANA

were found prior tonthe onset of iridocclitis. The presence of ANA should prove useful in identifying patients with juvenile **rheumatoid arthritis** at risk for chronic iridocyclitis. In contrast, negative tests for ANA in patients wit childhood onset arthritis and iridocyclitis were found to be associated with acute iridocyclitis and subsequent ankylosing spondylitis.

L9 ANSWER 22 OF 25 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
75023135 EMBASE Document No.: 1975023135. A study of the therapeutic value of
electrophoresis with **bee venom** ('mellivenon') in children with **rheumatoid arthritis** (Bulgarian).
Nikolova V.. Bulgaria. PROBL.PEDIAT. Vol.16/- (101-106) 1973.
CODEN: XXXXXB. Language: Bulgarian.

AB Mellivenon was introduced by electrophoresis into the affected joints of 18 children with **rheumatoid arthritis**. **Bee venom** is a complex mixture of biologic substances, including melletin, apamine, hyaluronidase and phospholipase A, which have a local analgesic, hyperemia inducing, and antiinflammatory effect and stimulate the pituitary adrenal system, followed by enhanced secretion of adrenal corticotrophic hormone and cortisone. Treatment was carried out, in conjunction with the maintenance antirheumatic drug therapy previously given for months without much effect. The untoward reactions were observed. The joint pains abated and even completely disappeared; joint deformities improved in 48 cases and the extent of movement in 39. Rheumatic activity was reduced in children with moderate and minimal activity, but was unaffected in severely active cases. With the exception of 2 patients with high rheumatoid activity whose basic inflammatory process was further activated, it was possible to reduce the dose of maintenance hormonal treatment in 4 patients, to discontinue it in 2 and to reduce all other antirheumatic therapy, aspirin, amidopyrine, analgin and resochin in 8 patients.

L9 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2001 ACS
1964:47957 Document No. 60:47957 Original Reference No. 60:8468c-d
Fingerprinting the hyaluronic acid component of normal and pathological synovial fluids. Barker, S. A.; Bayyuk, S. H. I.; Brimacombe, J. S.; Hawkins, C. F.; Stacey, M. (Univ. Birmingham, UK). Clin. Chim. Acta, 8(6), 902-9 (English) 1963.

AB Small amts. (about 1 mg.) of hyaluronic acid (I) from deproteinized synovial fluids from healthy persons and patients with **rheumatoid arthritis**, osteoarthritis, rheumatic fever, and other joint disorders were analyzed by titration with 0.05% cetylpyridinium chloride. The shape of the turbidity curves were specific for each type of I. Since progressive hydrolysis of I with **bee venom** hyaluronidase gave decreasing intensities of turbidity curves, it appeared that high specific turbidities were related to high mol. wts. and to high intrinsic viscosities. Therefore, the specific turbidity curves were unique for each sample of I.

L9 ANSWER 24 OF 25 MEDLINE
60054289 Document Number: 60054289. **Bee venom** in the treatment of infectious non-specific (**rheumatoid**) **arthritis**. PERTSULENKO V A. Sovet Med, (1961 Jun) 25 94-101.
Language: Russian.

L9 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2001 ACS
1948:4263 Document No. 42:4263 Original Reference No. 42:935e-i,936a-c
Synovial fluid mucin. Ropes, Marian W.; Robertson, Wm. v. B.; Rossmeisl, Elsie C.; Peabody, R. Barbara; Bauer, Walter (Harvard Med. School, Boston). Acta med. scand., 128(Suppl. 196), 700-44 (Unavailable) 1947.

AB The highly viscous protein-polyglucide complex mucin is principally of

mesodermal origin. Epithelial mucins differ from these in compn., appearance, and reaction to specific enzymes. Half-liter quantities of synovial fluid (cattle) were dild. to 2 l. and AcOH was added to 1%. The pptd. mucin was washed with H2O, redissolved in 0.05 M Na2HPO4 and repptd. with AcOH. Mucin is insol. in AcOH, alc., ether, or acetone; it is pptd. by tungstic acid, trichloroacetic acid, or heavy metals. It is salted out by 60% (NH4)2SO4, 22.5% Na2SO4, or by 2.3 M phosphate at pH 6.5. The polyglucide moiety is a white, fluffy, fibrous substance sol. in H2O, acids, or alkalies, but insol. in alc. or acetone. The most characteristic phys. property of mucin is the high viscosity which is largely due to the polyglucide portion. It is responsible for the viscosity of synovial fluid. The viscosity of its solns. does not vary directly with the concn. but an empirical relationship was found between the log of viscosity and the square root of concn. The presence of salts greatly reduces the viscosity of mucin or of polyglucide solns. The viscosity increases from pH 11 to pH 4 (isoelec. point of mucin), where the mucin ppts. out from soln., but it redissolves at pH 3.7 with a much lower viscosity. The viscosity is reversibly decreased with increasing temp. but the reduction of viscosity due to reduction in mol. size, resulting from enzymic degradation, is irreversible. In normal synovial fluid the polyglucide of the mucin is highly polymerized (high viscosity and large mol. wt.) but, when the mol. is split, the viscosity drops to about that of water, and with AcOH, instead of the tough ropey ppt., a progressively less cohesive material is formed. Such breakdown can be achieved by various bacterial enzymes, like hyaluronidase, or by nonbacterial enzymes (testicle, sperm, skin, cornea, leech heads, **bee venom**, etc.), and the viscosity can be decreased in vivo in a few min. The liberation of hexosamine and reducing substances by these agencies follows much slower (24-48 hrs.). Antiserums have been prepd. which can inhibit these changes in the mucin. Besides these enzymes there are other substances (ascorbic acid) which cause only an irreversible decrease in viscosity. All these induce the "spreading" phenomenon owing to increased permeability. The bacterial and tissue enzymes are specific for the mesothelial mucins (synovial fluid, vitreous humor), but not the epithelial mucins or chondroitinsulfuric acid. Normal synovial fluid does not show any hyaluronidase activity; it does contain 2 substances responsible for nonspecific in vitro decrease in mucin viscosity (ascorbic acid and alk. phosphatase) but there is no evidence of an in vivo breakdown of mucin. Joint diseases affect formation and destruction of mucin. Traumatic inflammation apparently stimulates formation of mucin by connective tissue cells. Abnormally high mucin concns. are found in certain pathol. conditions of the joints; also, a reduced viscosity per unit concn. of mucin indicates the occurrence of some breakdown. In **rheumatoid arthritis** the degradation of the mucin increases proportionally with the severity of the joint involvement with loss of viscosity. The changes in the mucin are frequently of great value in differential diagnosis or even in prognosis. Signs of marked degradation of mucin in synovial fluid tends to rule out any traumatic types of joint disease. The physiol. functions of mucin are discussed.

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L12 ANSWER 1 OF 6 SCISEARCH COPYRIGHT 2001 ISI (R)
2001:246415 The Genuine Article (R) Number: 409JZ. **Bee venom** injection into an acupuncture point reduces arthritis associated edema and nociceptive responses. Kwon Y B; Lee J D; Lee H J; Han H J; Mar W C; Kang S K; Beitz A J; Lee J H (Reprint). Seoul Natl Univ, Coll Vet Med, Dept Vet Physiol, Suwon 441744, South Korea (Reprint); Seoul Natl Univ, Sch Agr Biotechnol, Suwon 441744, South Korea; Kyung Hee Univ, Coll Oriental Med, Dept Acupuncture & Moxibust, Seoul, South Korea; Chonnam Natl Univ, Hormone Res Ctr, Kwangju, South Korea; Seoul Natl Univ, Inst Nat Prod Res, Seoul, South Korea; Univ Minnesota, Coll Vet Med, Dept Vet Pathobiol, St Paul, MN 55108 USA. PAIN (15 FEB 2001) Vol. 90, No. 3, pp. 271-280. Publisher: ELSEVIER SCIENCE BV. PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 0304-3959. Pub. country: South Korea; USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB **Bee venom** (BV) has traditionally been used in Oriental medicine to relieve pain and to treat inflammatory diseases such as rheumatoid arthritis (RA). While several investigators have evaluated the anti-inflammatory effect of BV treatment, the anti-nociceptive effect of BV treatment on inflammatory pain has not been examined. Previous studies in experimental animals suggest that the therapeutic effect of BV on arthritis is dependent on the site of administration. Because of this potential site specificity. the present study was designed to evaluate the anti-nociceptive effect of BV injections into a specific acupoint (Zusanli) compared to a non-acupoint in an animal model of chronic arthritis. Subcutaneous BV treatment (1 mg/kg pet day) was found to dramatically inhibit paw edema caused by Freund's adjuvant injection. Furthermore, BV therapy significantly reduced arthritis-induced nociceptive behaviors (i.e. the nociceptive scores for mechanical hyperalgesia and thermal hyperalgesia). These anti-nociceptive/anti-inflammatory effects of BV were observed from 12 days through 21 days post-BV treatment. In addition, BV treatment significantly suppressed adjuvant-induced Fos expression in the lumbar spinal cord at 3 weeks post-adjuvant injection. Finally, injection of BV into the Zusanli acupoint resulted in a significantly greater analgesic effect on arthritic pain as compared to BV injection in to a more distant non-acupoint. The present study demonstrates that BV injection into the Zusanli acupoint has both anti-inflammatory and anti-nociceptive effects on Freund's adjuvant-induced arthritis in rats. These findings raise the possibility that BV acupuncture may be a promising alternative medicine therapy for the long-term treatment of rheumatoid arthritis. (C) 2001 International Association for the Study of Pain. published by Elsevier Science B.V. All rights reserved.

L12 ANSWER 2 OF 6 MEDLINE DUPLICATE 1
2001485209 Document Number: 21418066. PubMed ID: 11527062. The analgesic

efficacy of **bee venom** acupuncture for knee **osteoarthritis**: a comparative study with needle acupuncture. Kwon Y B; Kim J H; Yoon J H; Lee J D; Han H J; Mar W C; Beitz A J; Lee J H. (Department of Veterinary Physiology, College of Veterinary Medicine and School of Agricultural Biotechnology, Seoul National University, Suwon, Korea.) AMERICAN JOURNAL OF CHINESE MEDICINE, (2001) 29 (2) 187-99. Journal code: 3E4; 7901431. ISSN: 0192-415X. Pub. country: United States. Language: English.

AB The aim of this investigation was to determine whether **bee venom** (BV) administered directly into an acupoint was a clinically effective and safe method for relieving the pain of patients with knee **osteoarthritis** (OA) as compared to traditional needle acupuncture. We evaluated the efficacy of BV acupuncture using both pain relief scores and computerized infrared thermography (IRT) following 4 weeks of BV acupuncture treatment. We observed that a significantly higher proportion of subjects receiving BV acupuncture reported substantial pain relief as compared with those receiving traditional needle acupuncture therapy. Furthermore, the IRT score was significantly improved and paralleled the level of pain relief.

L12 ANSWER 3 OF 6 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

1999206812 EMBASE Arthritis: New agents herald more effective symptom management. Simon L.S.. Dr. L.S. Simon, Graduate Medical Education, Beth Israel Deaconess Medical Center, Boston, MA, United States. Geriatrics 54/6 (37-44) 1999.
Refs: 15.
ISSN: 0016-867X. CODEN: GERIAZ. Pub. Country: United States. Language: English. Summary Language: English.

AB For physicians and patients alike, managing the symptoms of rheumatoid and **osteoarthritis** is an ongoing challenge. Myriad therapies are available, virtually all provide only temporary relief and produce side effects that interrupt long-term use. New disease-modifying antirheumatic drugs, biologic response modifiers, and cyclooxygenase inhibitors offer the promise of more effective, longer lasting symptom management and, in some cases, reduced side effects. The population of older persons affected by arthritis continues to grow. Increased familiarity with these new treatments will aid primary care physicians in helping older patients better manage their arthritis during the next decade.

L12 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS

1989:429996 Document No.: BA88:88254. **BEE VENOM** THERAPY FOR ARTHRITIS. KIM C M. MONMOUTH PAIN INST. INC., RED BANK, N.J., U.S.A. 07701.. RHUMATOLOGIE, (1989) 41 (3), 67-72. CODEN: RHUMAY. Language: English.

AB **Bee Venom** therapy for arthritis remains somewhat controversial. Unfortunately, there are very few controlled studies available to guide clinical practice. One Hundred and Eight patients with longstanding history of arthritis (RA or OA) who failed to respond to conventional medical treatment were used as subjects (Sept. 85 to Sept. 87). Participation was on a voluntary basis as denoted by informed consents from all subjects. All subjects were tested for possible allergic reaction before initial treatment. 0.1 ml. standard BV-10 was injected intradermally twice a week. The number of injections increased gradually each subsequent treatment until evaluation showed markedly improved or completely resolved. Pain was most common problem with subjects. Pain measure included the McGill Pain Questionnaire and Visual Analog Scales. Clinical evaluation included serial physical examinations and the thermographic findings. Each subject was followed 6 months to 2 years after finished treatment. Most of subjects, showed slight improvements after 3rd session and marked improvement average 12th treatment. Total 33,644 injections were given. No clinical complications or serious side

effects were observed in any subjects who participated in the study. It was concluded the **bee venom** therapy is safe, effective and has no serious side effects, as long as a person is not allergic to **bee venom**. The preliminary results highly suggest that **bee venom** therapy is a new alternative approach for arthritis victims who failed to respond to the conventional medical treatments.

L12 ANSWER 5 OF 6 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
84066648 EMBASE Document No.: 1984066648. [Results and difficulties in treatment of rheumatic disease with injections of **bee-venom** extract]. RESULTATS ET DIFFICULTES DE TRAITEMENT DE CERTAINS RRHUMATISANTS PAR LES INJECTIONS D'EXTRAIT DE VENIN D'ABEILLE. Palmer M.; Forestier F.. France. Rhumatologie 35/6 (289-291) 1983. CODEN: RHUMAY. Pub. Country: France. Language: French.

L12 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2001 ACS
1964:47957 Document No. 60:47957 Original Reference No. 60:8468c-d Fingerprinting the hyaluronic acid component of normal and pathological synovial fluids. Barker, S. A.; Bayyuk, S. H. I.; Brimacombe, J. S.; Hawkins, C. F.; Stacey, M. (Univ. Birmingham, UK). Clin. Chim. Acta, 8(6), 902-9 (English) 1963.
AB Small amts. (about 1 mg.) of hyaluronic acid (I) from deproteinized synovial fluids from healthy persons and patients with rheumatoid arthritis, **osteoarthritis**, rheumatic fever, and other joint disorders were analyzed by titration with 0.05% cetylpyridinium chloride. The shape of the turbidity curves were specific for each type of I. Since progressive hydrolysis of I with **bee venom** hyaluronidase gave decreasing intensities of turbidity curves, it appeared that high specific turbidities were related to high mol. wts. and to high intrinsic viscosities. Therefore, the specific turbidity curves were unique for each sample of I.

=> s l3 and gouty arthritis

L13 0 L3 AND GOUTY ARTHRITIS

=> s l3 and psoriatic arthritis

L14 0 L3 AND PSORIATIC ARTHRITIS

=> s l3 and psoriasis

L15 6 L3 AND PSORIASIS

=> dup remove l15

PROCESSING COMPLETED FOR L15
L16 4 DUP REMOVE L15 (2 DUPLICATES REMOVED)

=> d l16 1-4 cbib abs

L16 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2001 ACS
2000:841977 Document No. 134:25351 Heterocyclic phospholipase A2-specific inhibitors, their preparation, their use in treatment of inflammation, and pharmaceutical and cosmetic compositions containing them. Assogba, Leon; Heymans, Francoise; Dong, Chang-Zhi; Godfroid, Jean-Jacques (Universite Paris 7 - Denis Diderot, Fr.). PCT Int. Appl. WO 2000071118 A1 20001130, 64 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,

BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (French). CODEN: PIXXD2. APPLICATION: WO 2000-FR1386 20000519. PRIORITY: FR 1999-6366 19990519.

AB The invention provides phospholipase A2 inhibitor heterocyclic compds. (Markush included). The compds. are capable of acting on PLA2 and are advantageously secreted nonpancreatic PLA2-specific inhibiting compds. completely inactive towards pancreatic PLA2. The invention also provides a method for prepg. the compds., pharmaceutical and cosmetic compns. contg. them, and their use in particular for treating inflammatory pathologies.

L16 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2001 ACS

2000:191197 Document No. 132:232740 Protein and cDNA sequences of honey **bee venom** protein PX3.101, and uses thereof in the treatment of various diseases. Cui, Xiangmin; Lu, Yuefeng (Pan Pacific Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2000015774 A1 20000323, 80 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US21077 19990913. PRIORITY: US 1998-100172 19980914.

AB The invention provides protein and cDNA sequences of a novel protein, PX3.101, which can be isolated from honey **bee venom**. The invention also provides pharmaceutical compns. based upon PX3.101 polypeptide and methods for using same in the treatment of various diseases, including various inflammatory diseases such as rheumatoid arthritis. The invention further relates to the treatment of diseases assocd. with chemokine (esp. IL-8) imbalances, wherein PX3.101 inhibits the binding of a chemokine with its receptor.

L16 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2001 ACS

1996:756546 Document No. 126:17804 Human antibodies derived from immunized xenomice. Kucherlapati, Raju; Jakobovits, Aya; Klapholz, Sue; Brenner, Daniel G.; Capon, Daniel J. (Cell Genesys, Inc., USA). PCT Int. Appl. WO 9634096 A1 19961031, 64 pp. DESIGNATED STATES: W: AU, CA, FI, HU, JP, KR, NO, NZ; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US5500 19950428.

AB Antibodies with fully human variable regions against a specific antigen can be prepd. by administering the antigen to a transgenic animal which has been modified to produce such antibodies in response to antigenic challenge, but whose endogenous loci have been disabled. Various subsequent manipulations can be performed to obtain either antibodies per se or analogs thereof.

L16 ANSWER 4 OF 4 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1

81150838 EMBASE Document No.: 1981150838. **Bee venom** in composite treatment of **psoriasis**. Kozhukhar G.S.. Kaf. Kozhn. Ven. Bol., Med. Inst., Kiev, Ukraine. Vestnik Dermatologii i Venerologii 57/4 (52-54) 1981.
CODEN: VDVEAV. Pub. Country: Russia. Language: Russian.

=> s l3 and ankylosing spondylitis

L17 1 L3 AND ANKYLOSING SPONDYLITIS

=> d l17 cbib abs

L17 ANSWER 1 OF 1 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
75096141 EMBASE Document No.: 1975096141. The association of antinuclear antibodies with the chronic iridocyclitis of juvenile rheumatoid arthritis
(Still's disease). Schaller J.G.; Johnson G.D.; Holborow E.J.; et al.. MRC
Rheum. Unit, Canadian Red Cross Mem. Hosp., Maidenhead, United Kingdom.
Arthritis and Rheumatism 17/4 (409-416) 1974.
CODEN: ARHEAW. Language: English.
AB Positive tests for antinuclear antibodies (ANA) were found in 51 of 58 (88%) patients with chronic iridocyclitis and juvenile rheumatoid arthritis (Still's 26111w13=more. disease). Antinuclear antibodies were predominantly of the IgG class of immunoglobulins and were generally present in titers of 1:50 (6 ANA units) or more, They were unassociated with disease activity, severety or duration, age of patient at onset or testing, or sex. Neither other autoantibodies nor antibodies reactive with
DNA or RNA were associated. In 8 patients tested early in disease, ANA were found prior tonthe onset of iridocclitis. The presence of ANA should prove useful in identifying patients with juvenile rheumatoid arthritis at
risk for chronic iridocyclitis. In contrast, negative tests for ANA in patients wit childhood onset arthritis and iridocyclitis were found to be associated with acute iridocyclitis and subsequent **ankylosing spondylitis**.

=> s l3 and fibromyalgia

L18 0 L3 AND FIBROMYALGIA

=> s l3 and fibromyositis

L19 0 L3 AND FIBROMYOSITIS

=> s l3 and myofascial dysfunction pain syndrome

L20 0 L3 AND MYOFASCIAL DYSFUNCTION PAIN SYNDROME

=> s l3 and tennis elbow

L21 0 L3 AND TENNIS ELBOW

=> s l3 and frozen shoulder

L22 0 L3 AND FROZEN SHOULDER

=> s l3 and bursitis

L23 0 L3 AND BURSITIS

=> s l3 and tendonitis

L24 0 L3 AND TENDONITIS

=> s l3 and inflammation

L25 198 L3 AND INFLAMMATION

```
=> dup remove l25

PROCESSING COMPLETED FOR L25
L26          116 DUP REMOVE L25 (82 DUPLICATES REMOVED)

=> s l26 and soft tissue

L27            0 L26 AND SOFT TISSUE

=> s l26 and neuritis

L28            0 L26 AND NEURITIS

=> s l3 and neuralgia

L29            2 L3 AND NEURALGIA

=> dup remove l29

PROCESSING COMPLETED FOR L29
L30            2 DUP REMOVE L29 (0 DUPLICATES REMOVED)

=> d l30 1-2 cbib abs


L30  ANSWER 1 OF 2  EMBASE  COPYRIGHT 2001 ELSEVIER SCI. B.V.
94310009  EMBASE  Document No.: 1994310009. 'Bee Sting therapy': The revival
of
     a dangerous practice [4]. Altomare G.F.; Capella G.L.. Istituto di
     Dermatologia, Via Pace 9,20122 Milan, Italy. Acta Dermato-Venereologica
     74/5 (409)  1994.
     ISSN: 0001-5555. CODEN: ADVEA4. Pub. Country: Norway. Language: English.

L30  ANSWER 2 OF 2  BIOSIS  COPYRIGHT 2001 BIOSIS
1987:391087  Document No.: BR33:71227. BEE VENOM THERAPY
     FOR ARTHRITIS AND NEURALGIAS. KIM C M. MONMOUTH PAIN INST., 46
     ENGLISH PLAZA, RED BANK, N.J.. FIFTH WORLD CONGRESS ON PAIN, HAMBURG,
WEST
     GERMANY, AUGUST 2-7, 1987. PAIN. (1987) 0 (SUPPL 4), S262. CODEN: PAINDB.
     ISSN: 0304-3959. Language: English.


=> s l3 and neuralgia

L31            2 L3 AND NEURALGIA

=> dup remove l31

PROCESSING COMPLETED FOR L31
L32            2 DUP REMOVE L31 (0 DUPLICATES REMOVED)

=> d his


     (FILE 'HOME' ENTERED AT 12:12:23 ON 05 DEC 2001)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 12:12:39 ON
     05 DEC 2001
L1             25 S ADMINSTERING
L2              0 S L1 AND BEE VENOM
L3           7626 S BEE VENOM
L4             14 S L3 AND ANESTHETIC
L5             10 DUP REMOVE L4 (4 DUPLICATES REMOVED)
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L6            2 S L3 AND COADMINISTRATION
L7            2 DUP REMOVE L6 (0 DUPLICATES REMOVED)
L8           43 S L3 AND RHEUMATOID ARTHRITIS
L9           25 DUP REMOVE L8 (18 DUPLICATES REMOVED)
L10           0 S L3 AND OSTOARTHRITIS
L11           8 S L3 AND OSTEOARTHRITIS
L12           6 DUP REMOVE L11 (2 DUPLICATES REMOVED)
L13           0 S L3 AND GOUTY ARTHRITIS
L14           0 S L3 AND PSORIATIC ARTHRITIS
L15           6 S L3 AND PSORIASIS
L16           4 DUP REMOVE L15 (2 DUPLICATES REMOVED)
L17           1 S L3 AND ANKYLOSING SPONDYLITIS
L18           0 S L3 AND FIBROMYALGIA
L19           0 S L3 AND FIBROMYOSITIS
L20           0 S L3 AND MYOFASCIAL DYSFUNCTION PAIN SYNDROME
L21           0 S L3 AND TENNIS ELBOW
L22           0 S L3 AND FROZEN SHOULDER
L23           0 S L3 AND BURSITIS
L24           0 S L3 AND TENDONITIS
L25         198 S L3 AND INFLAMMATION
L26         116 DUP REMOVE L25 (82 DUPLICATES REMOVED)
L27           0 S L26 AND SOFT TISSUE
L28           0 S L26 AND NEURITIS
L29           2 S L3 AND NEURALGIA
L30           2 DUP REMOVE L29 (0 DUPLICATES REMOVED)
L31           2 S L3 AND NEURALGIA
L32           2 DUP REMOVE L31 (0 DUPLICATES REMOVED)

=> s l26 and migraine

L33           0 L26 AND MIGRAINE

=> s l3 and migraine

L34           2 L3 AND MIGRAINE

=> dup remove l34

PROCESSING COMPLETED FOR L34
L35           2 DUP REMOVE L34 (0 DUPLICATES REMOVED)

=> d l35 1-2 cbib abs


L35  ANSWER 1 OF 2  EMBASE  COPYRIGHT 2001 ELSEVIER SCI. B.V.
1998132614  EMBASE  Complementary medicine homoeopathy. Barnes J..
     Pharmaceutical Journal  260/6988 (492-497)  4 Apr 1998.
     Refs: 44.
     ISSN: 0031-6873. CODEN: PHJOAV. Pub. Country: United Kingdom. Language:
     English.

L35  ANSWER 2 OF 2  BIOSIS  COPYRIGHT 2001 BIOSIS
1982:137971  Document No.: BR23:67963. ADENINE NUCLEOTIDES AND NUCLEOSIDES IN
     HYPOXIA. BURNSTOCK G. LONDON, ENGLAND.. SYMPOSIUM ON CEREBRAL HYPOXIA IN
     THE PATHOGENESIS OF MIGRAINE ATTACKS, BRIGHTON, SUSSEX, ENGLAND, SEPT.
     3-4, 1981. DRUGS TODAY. (1981 (RECD 1982)) 17 (12), 570-571. CODEN:
     DRTOBK. Language: English.


=> s l3 and eczema

L36          13 L3 AND ECZEMA

=> dup remove l36
```

PROCESSING COMPLETED FOR L36
L37 10 DUP REMOVE L36 (3 DUPLICATES REMOVED)

=> d l37 1-10 cbib abs

L37 ANSWER 1 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
2001306358 EMBASE A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Johansson S.G.O.; Hourihane J.O'B.; Bousquet J.; Bruijnzeel-Koomen C.; Dreborg S.; Haahtela T.; Kowalski M.L.; Mygind N.; Ring J.; Van Cauwenberge P.; Van Hage-Hamsten M.; Wuthrich B.. Prof. S.G.O. Johansson, Department of Medicine, Unit of Clinical Immunology, Karolinska Hospital, SE-171 76 Stockholm, Sweden. Allergy: European Journal of Allergy and Clinical Immunology 56/9 (813-824) 2001.
Refs: 107.
ISSN: 0105-4538. CODEN: LLRGDY. Pub. Country: Denmark. Language: English. Summary Language: English.
AB This report has been prepared by an EAACI task force representing the five EAACI Sections and the EAACI Executive Committee composed of specialists that reflect the broad opinion on allergy expressed by various clinical and basic specialties dealing with allergy. The aim of this report is to propose a revised nomenclature for allergic and related reactions that can be used independently of target organ or patient age group. The nomenclature is based on the present knowledge of the mechanisms which initiate and mediate allergic reactions. However, the intention has not been to revise the nomenclature of nonallergic hypersensitivity.

L37 ANSWER 2 OF 10 SCISEARCH COPYRIGHT 2001 ISI (R)
2001:586457 The Genuine Article (R) Number: 449AA. Allergen immnunotherapy in allergic diseases with special regard to atopic **eczema**. Hirsch T (Reprint). Tech Univ Dresden, Fak Med, Klin & Poliklin Kinderheilkunde, Fetscherstasse 74, D-01307 Dresden, Germany (Reprint); Tech Univ Dresden, Fak Med, Klin & Poliklin Kinderheilkunde, D-01307 Dresden, Germany.
MONATSSCHRIFT KINDERHEILKUNDE (JUN 2001) Vol. 149, No. 6, pp. 554-+.
Publisher: SPRINGER-VERLAG. 175 FIFTH AVE, NEW YORK, NY 10010 USA. ISSN: 0026-9298. Pub. country: Germany. Language: German.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB According to modern concepts allergen immunotherapy influences the capacity of allergen specific T cells to react to allergen presentation. Subcutaneous immunotherapy with allergen extracts has been shown to be superior to placebo in the treatment of allergic rhinoconjunctivitis and allergic asthma. Because the treatment does not interfere with other antiinflammatory and symptomatic treatments of asthma and rhinoconjunctivitis it is an additional treatment option in child ren aged 5 years and older in whom allergen exposure is an im porta nt determinant of the course of the disease. As yet, there is no sufficient data to recommend allergen immunotherapy in the treatment of atopic **eczema** . However, allergen immunotherapy for rhinoconjunctivitis or asthma is not contraindicated if atopic **eczema** is present If allergy to hymenoptera venom leads to life-threatening symptoms,specific immunotherapy is indicated absolutely even in children below the age of 5 years.

L37 ANSWER 3 OF 10 MEDLINE
1999075579 Document Number: 99075579. PubMed ID: 9860236. IgE antibodies specific for carbohydrates in a patient allergic to gum arabic (Acacia senegal). Fotisch K; Fah J; Wuthrich B; Altmann F; Haustein D; Vieths S.

(Department of Allergology, Paul-Ehrlich-Institute, Langen, Germany.) ALLERGY, (1998 Nov) 53 (11) 1043-51. Journal code: 39C; 7804028. ISSN: 0105-4538. Pub. country: Denmark. Language: English.

AB The present study deals with the detailed investigation of the IgE antibody response of a gum arabic-allergic patient. The patient showed multiple serologic and skin test sensitizations to a range of pollen, other inhalants and foods, and **bee venom**, and to the recombinant allergens Bet v 1 and Bet v 2. Moreover, the patient's serum reacted strongly to gum-arabic extract. The NaIO4-treated and thus deglycosylated extract showed no binding to IgE. In contrast, removal of the protein backbone by basic hydrolysis did not deplete the IgE reactivity. Therefore, it is concluded that the gum arabic-specific IgE antibodies of this patient were mainly directed against the carbohydrate fraction of this material. In IgE-inhibition assays, cross-reactions occurred in the range of 60% between gum arabic and known immunogenic N-glycans containing alpha1-3-linked fucose. Since the inhibition graphs were not parallel and the inhibition was not complete with heterologue antigens, the cross-reacting epitopes of gum arabic appeared to be different from the latter well-known cross-reactive carbohydrate determinants (CCD). Inhibition may have been caused by a partial immunologic identity of the investigated carbohydrate moieties. A strong IgE response to the fucose-containing glycan from bromelain was measured in a glycan ELISA that utilizes purified glycopeptides at the solid phase.

This response, which may explain the multiple sensitizations without clinical significance diagnosed in the patient, could originate from inhalation of pollen, which is known to contain similar glycans, or from occupational sensitization during work as a baker and confectioner. Since the gum-arabic protein showed only very weak participation in the IgE reactivity, the clinical symptoms of the patient caused by gum arabic may be attributed to carbohydrate epitopes. Due to the repetitive polysaccharide sequence of gum arabic, several epitopes for the cross-linking of IgE should exist.

L37 ANSWER 4 OF 10 MEDLINE DUPLICATE 1

96434734 Document Number: 96434734. PubMed ID: 8837658. IgE antibodies to

Hymenoptera venoms in the serum are common in the general population and are related to indications of atopy. Schafer T; Przybilla B. (Hautklinik am Universitatskrankenhaus Eppendorf, Hamburg, Germany.) ALLERGY, (1996 Jun) 51 (6) 372-7. Journal code: 39C; 7804028. ISSN: 0105-4538. Pub. country: Denmark. Language: English.

AB Determination of Hymenoptera venom (HV)-specific serum IgE antibodies is a

useful diagnostic method in patients with systemic anaphylactic reaction (SAR) to Hymenoptera stings. In a general population cohort, we determined

the prevalence of SAR and HV-specific IgE antibodies and assessed parameters associated with the latter. A total of 277 voluntarily participating inhabitants of rural Bavaria (Germany) (232 adults, mean age

38.0 years; 45 children, mean age 8.4 years) were investigated for a history of atopic disease or SAR to insect stings; in 258 of these, total IgE and specific IgE antibodies to HV (Apis mellifera, Vespula vulgaris/germanica) and four common aeroallergens (birch pollen, grass pollen, house-dust mite, and cat dander) in the serum were determined. Nine (3.3%) subjects reported SAR to insect stings. In 27.1% of the sera, specific IgE antibodies to HV were found, to **bee venom** in 24.8%, and to wasp venom in 8.5% ($P < 0.0001$). Of those exhibiting HV-specific IgE, 7.1% reported SAR to insect stings. A personal history of

atopic disease (hay fever, asthma, or atopic **eczema**) was present in 16.7%, specific IgE to common aeroallergens was found in 32.6%, and total IgE > 100 kU/l was found in 22.5%. Specific serum IgE to HV was

significantly associated with male sex (female vs. male, OR = 0.47; CI 0.25-0.86), young age (children vs. adults, OR = 2.80; CI 1.25-6.28), a history of SAR to insect stings (OR = 4.16; CI 1.15-15.03), total sIgE > 100 kU/l (OR = 3.88; CI 1.98-7.60), and specific IgE antibodies to three of the four aeroallergens (grass pollen, OR = 7.24 CI 3.66-14.38; birch pollen, OR = 3.67 CI 1.54-8.81; and house-dust mite, OR = 4.61 CI 2.08-10.32). It is concluded that immunologic sensitization to HV is common in the general population and is associated with atopy-related humoral IgE hyperresponsiveness.

L37 ANSWER 5 OF 10 SCISEARCH COPYRIGHT 2001 ISI (R)
92:522662 The Genuine Article (R) Number: JL095. PHOSPHOLIPASE-A2 INHIBITION BY ALKYLBENZOYLACRYLIC ACIDS. KOHLER T; HEINISCH M; KIRCHNER M; PEINHARDT
G; HIRSCHELMANN R; NUHN P (Reprint). MARTIN LUTHER UNIV, DEPT PHARM, WEINBERGWEG 15, O-4010 HALLE, GERMANY (Reprint); UNIV TUBINGEN, PHARM, W-7400 TUBINGEN 1, GERMANY. BIOCHEMICAL PHARMACOLOGY (18 AUG 1992) Vol. 44, No. 4, pp. 805-813. ISSN: 0006-2952. Pub. country: GERMANY. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB 3-(4-Alkylbenzoyl)acrylic acids (ABAAs) were synthesized by acylation of alkylbenzenes with maleic anhydride and then screened in vitro for inhibition of phospholipase A2 (PLA2) from snake venom and from porcine pancreas. The inhibitory potency of ABAAs increased with the length of the
alkyl residues resulting in IC50 values of between 10(-7) and 10(-4) mol/L. The most potent inhibitors of the snake venom PLA2 were the 4-(n)-hexadecyl and octadecyl (OBAA) derivatives. Kinetic experiments referred to a time-dependent inhibitory reaction. Irreversibility was examined by dilution and dialysis. A molar ratio of inactivation of OBAA of nearly 20 was estimated. Double reciprocal replots of the apparent inactivation constants to the concentration of OBAA gave a (pseudo) first order rate constant of inactivation of 2.3 min-1. For the dissociation constant of the enzyme-inhibitor intermediate, a value of 6 x 10(-6) mol/L
was obtained. On the other hand, the PLA2 from porcine pancreas seemed hardly to be inhibited by ABAAs. The present data are discussed in relation to the proposed model for PLA2 inactivation by manoalide. In human PMNs leukotriene B4 and 5-HETE production was essentially reduced. In human platelets the thrombin-induced TxA2 production was reduced. Since
these effects disappeared after addition of arachidonic acid, these findings refer to a PLA2 inhibition. The immunologically induced bronchospasm in guinea pigs was significantly and dose-dependently inhibited by OBAA. This indicates that ABAAs might be useful in treating allergic diseases, such as asthma, **eczema**, allergic shock and others.

L37 ANSWER 6 OF 10 MEDLINE
93020631 Document Number: 93020631. PubMed ID: 1404018. Allergy: conventional and alternative concepts. Summary of a report of the Royal College of Physicians Committee on Clinical Immunology and Allergy. Anonymous. JOURNAL OF THE ROYAL COLLEGE OF PHYSICIANS OF LONDON, (1992 Jul) 26 (3) 260-4. Journal code: JVB; 7503108. ISSN: 0035-8819. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Allergy is an exaggerated response of the immune system to external substances. It plays a role in a wide range of diseases. In some, such as summer hayfever, the symptoms are entirely due to allergy. In other conditions, particularly asthma, **eczema** and urticaria, allergy plays a part in some patients but not all. In these situations, allergy may either have a major role or provide just one of many triggers. In an individual patient's illness, the importance of allergy may change with time. The most common allergens (substances causing allergy) are grass and

tree pollens, the house dust mite, products from pets and other animals, agents encountered in industry, wasp and **bee venom**, drugs, and certain foods. Food allergy presents a particularly difficult problem. Some individuals who react to food suffer from true food allergy but in others there is no evidence of an alteration in the immune system. Here the term 'food intolerance' is preferable. Conventional doctors treat allergy by allergen avoidance--where this is possible--and drugs that relieve symptoms. In a few selected cases, in which other methods have failed, immunotherapy (desensitisation or hyposensitisation) is recommended. Patients who consult practitioners of alternative allergy often do so because they are dissatisfied with the conventional approach to diagnosis and treatment, and sometimes because they have conditions which conventional doctors do not accept as having an allergic basis. There is a very wide range of alternative approaches to allergy, including the methods used by clinical ecologists, acupuncturists and homoeopathists. Hypnosis may have a small role to play in asthma, and similar claims for acupuncture need to be evaluated.(ABSTRACT TRUNCATED AT 250 WORDS)

L37 ANSWER 7 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

92326037 EMBASE Document No.: 1992326037. Allergy: Conventional and alternative concepts. A report of the Royal College of Physicians Committee on Clinical Immunology and Allergy. Kay A.B.; Lessof M.H.. Royal College of Physicians, 11 St. Andrew's Place,London NW1 4LE, United Kingdom. Clinical and Experimental Allergy, Supplement 22/3 (i-44) 1992.

ISSN: 0960-2178. CODEN: CLASEN. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Allergy is an exaggerated response of the immune system to external substances. It plays a role in a wide range of diseases. In some, such as summer hayfever, the symptoms are due entirely to allergy. In other conditions, particularly asthma, **eczema** and urticaria, allergy plays a part in some patients but not all. In these situations, allergy may have either a major role or provide just one of many triggers. In an individual patient's illness, the importance of allergy may change with time. The most common allergens (substances causing allergy) are grass and tree pollens, the house dust mite, products from pets and other animals, agents encountered in industry, wasp and **bee venom**, drugs, and certain foods. Food allergy presents a particularly difficult problem. Some individuals who react to food suffer from food allergy in its strict sense but in others there is no evidence of an alteration in the immune system. Here the term 'food intolerance' is preferable. Conventional doctors treat allergy by allergen avoidance - where this is possible - and drugs that relieve symptoms. In a few selected cases, in which other methods have failed, immunotherapy (desensitisation or hyposensitisation) is recommended. Although patients who consult practitioners of alternative allergy may do so by preference, it is often also because they are dissatified with the conventional approach to diagnosis and treatment, or because they have conditions which conventional doctors do not accept as having an allergic basis. There is a very wide range of alternative approaches to allergy, including the methods used by clinical ecologists and other treatments such as acupuncture and homoeopathy. Hypnosis may have a small role to play in helping the asthmatic and similar effects have been suggested for acupuncture. Furthermore, it is likely that there are still many active ingredients in medicinal plants used by herbalists but these need to be clearly identified and purified before their usefulness can be evaluated properly. Apart from these situations, we have yet to be convinced by

substantial evidence that any of the other alternative methods of diagnosing or treating allergic disease are of proven value. There have, however, been many false and misleading claims and serious harm may be caused by misdiagnosis or delays in appropriate treatment. The public should be warned against costly methods of diagnosis and treatment which have not been validated. It is clear that many patients improve as a result of suggestion or the 'placebo response'. The placebo response can be very powerful and for this reason it requires further scientifically based research since a better understanding of the interplay between the brain and allergy-associated symptoms might result in improved forms of therapy. On the other hand, the placebo response must be clearly distinuished from the effects claimed for a particular form of treatment. Allergic diseases are common and the cause of much ill health. Improvements in diagnosis and treatment of allergy, like other branches of medicine, can only be made by rigorous clinical scientific studies.

L37 ANSWER 8 OF 10 MEDLINE

93045686 Document Number: 93045686. PubMed ID: 1422946. Allergy. Conventional and alternative concepts. A report of the Royal College of Physicians Committee on Clinical Immunology and Allergy. Kay A B; Lessof M H. CLINICAL AND EXPERIMENTAL ALLERGY, (1992 Oct) 22 Suppl 3 1-44. Ref: 104. Journal code: CEB; 8906443. ISSN: 0954-7894. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Allergy is an exaggerated response of the immune system to external substances. It plays a role in a wide range of diseases. In some, such as summer hayfever, the symptoms are due entirely to allergy. In other conditions, particularly asthma, **eczema** and urticaria, allergy plays a part in some patients but not all. In these situations, allergy may have either a major role or provide just one of many triggers. In an individual patient's illness, the importance of allergy may change with time. The most common allergens (substances causing allergy) are grass and tree pollens, the house dust mite, products from pets and other animals, agents encountered in industry, wasp and **bee venom**, drugs, and certain foods. Food allergy presents a particularly difficult problem. Some individuals who react to food suffer from food allergy in its strict sense but in others there is no evidence of an alteration in the immune system. Here the term 'food intolerance' is preferable. Conventional doctors treat allergy by allergen avoidance--where this is possible--and drugs that relieve symptoms. In a few selected cases, in which other methods have failed, immunotherapy (desensitisation or hyposensitisation) is recommended. Although patients who consult practitioners of alternative allergy may do so by preference, it is often also because they are dissatisfied with the conventional approach to diagnosis and treatment, or because they have conditions which conventional doctors do not accept as having an allergic basis. There is a very wide range of alternative approaches to allergy, including the methods used by clinical ecologists and other treatments such as acupuncture and homoeopathy. Hypnosis may have a small role to play in helping the asthmatic and similar effects have been suggested for acupuncture. Furthermore, it is likely that there are still many active ingredients in medicinal plants used by herbalists but these need to be clearly identified and purified before their usefulness can be evaluated properly. Apart from these situations, we have yet to be convinced by substantial evidence that any of the other alternative methods of diagnosing or treating allergic disease are of proven value. There have, however, been many false and misleading claims and serious harm may be caused by misdiagnosis or delays in appropriate treatment. The public should be warned against costly methods of diagnosis and treatment which have not been validated.(ABSTRACT TRUNCATED AT 400 WORDS)

L37 ANSWER 9 OF 10 MEDLINE
83149518 Document Number: 83149518. PubMed ID: 6219557. Allergy in beekeepers. Bousquet J; Menardo J L; Michel F B. ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1982 Sep-Oct) 10 (5) 395-8. Journal code: 3AH; 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.
AB Beekeepers represent a high-risk group for allergic disorders. They are affected by beestings but only a very limited fraction of the population develops severe anaphylactic symptoms. On the other hand several beekeepers have slight anaphylactic symptoms when they start working. Immunologically they are like "spontaneously desensitized subjects". They often have **bee-venom** specific IgE and all of them have very high titers of **bee-venom** specific IgG. Beekeepers may present an atopic sensitization to bee-hive dust and develop asthma and rhinitis. Finally, they may present a contact dermatitis to a bee-product: the propolis. This type of allergy is not very frequent.

L37 ANSWER 10 OF 10 MEDLINE
79129631 Document Number: 79129631. PubMed ID: 422284. Comparison of the atopic background between allergic and non-allergic beekeepers. Miyachi S;
Lessof M H; Kemeny D M; Green L A. INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1979) 58 (2) 160-6. Journal code: GP9; 0404561. ISSN: 0020-5915. Pub. country: Switzerland. Language: English.
AB A study was carried out on beekeepers and their families. 34 subjects with a history of bee sting allergy and also a positive radioallergosorbent test (RAST) to honey **bee venom** were compared with 47 subjects with neither. 16 subjects in the bee allergy group (47%) had a history of atopic diseases as compared to 6 (13%) in the control group (p less than 0.01). 15 in the bee allergy group (44%) had at least one positive RAST to three common inhalant allergens as compared to 5 (11%) in the control group (p less than 0.01). These results suggest that, although bee sting allergy frequently affects non-atopic subjects, sensitization among beekeepers and their families occurs more readily in atopics. It is notable that a large proportion of patients injected with foreign proteins (the control group) either never develop venom-specific IgE antibodies or have suppressed their production.

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L38 16 L3 AND MULTIPLE SCLEROSIS

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=> d l39 1-12 cbib abs

L39 ANSWER 1 OF 12 SCISEARCH COPYRIGHT 2001 ISI (R)
2001:747598 The Genuine Article (R) Number: 471VM. Allergen-derived T cell peptide-induced late asthmatic reactions precede the induction of antigen-specific hyporesponsiveness in atopic allergic asthmatic subjects.
Oldfield W L G; Kay A B (Reprint); Larche M. Natl Heart & Lung Inst, Imperial Coll Sch Med, Dept Allergy & Clin Immunol, Dovehouse St, London SW3 6LY, England (Reprint); Natl Heart & Lung Inst, Imperial Coll Sch Med, Dept Allergy & Clin Immunol, London SW3 6LY, England. JOURNAL OF

IMMUNOLOGY (1 AUG 2001) Vol. 167, No. 3, pp. 1734-1739. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA. ISSN: 0022-1767. Pub. country: England. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Allergen-derived peptides can induce T cell tolerance in naive and Ag-primed mice. This is preceded by transient T cell activation. In humans, intradermal administration of short allergen-derived T cell peptide epitopes provokes IgE-independent isolated late asthmatic reactions (LARs) in sensitized subjects. In this study, we determine whether, as in mouse models, such peptides produce hyporesponsiveness to rechallenge with peptides, or whole allergen, either clinically or in terms of in vitro T cell responses. We found that a second injection of cat allergen (Fel d 1)-derived T cell peptides was associated with a marked reduction, or absence, of the LAR, and that up to 40 wk was required for return to baseline values. The cutaneous late-phase reaction to whole cat dander was also inhibited, even in subjects who did not experience an initial LAR. These observations were associated with a significant decrease in peptide- and whole allergen-induced proliferation of PBMCs and the production of IL-4, IL-13, and IFN-gamma in cultures. Thus, allergen-derived peptides induce tolerance to subsequent peptide injection in the target organ (the lung), reduce late-phase cutaneous responsiveness to whole allergen, and alter in vitro T cell reactivity.

L39 ANSWER 2 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
2001064397 EMBASE **Bee-venom** therapy for treating **multiple sclerosis**: A clinical trial. Hauser R.A.; Daguio M.; Wester D.; Hauser M.; Kirchman A.; Skinkis C.. Dr. R.A. Hauser, Caring Med. and Rehabilitation Svcs., Beulah Land Natural Medicine Clinic, Thebes, IL, United States. Alternative and Complementary Therapies 7/1 (37-45) 2001.
Refs: 16.
ISSN: 1076-2809. CODEN: ACTHFZ. Pub. Country: United States. Language: English. Summary Language: English.

AB MS; from its initial attack, can progress from being merely a nuisance to becoming a severely debilitating disease in its later stages. Little is understood about its causation, etiology, and biochemical progression within the body. New hypotheses continue to proliferate, implicating CD4 T-cells, interleukins, and viral susceptibility; yet, none have been proven. Before substantial progress can be achieved in MS research, scientists must identify this disease's specific etiology. This would allow the medical field to target pharmacotherapy to the specific disease etiology. Until this is accomplished, treatment remains merely guesswork. Therapeutic **bee-venom** injections on patients with MS, according to the results of this study, are effective in decreasing a patient's functional debilitation caused by the disease. The ROSS survey, using Friedman nonparametric statistical analysis showed significant improvements in balance, coordination, bladder and bowel control, upper- and lower-extremity strength, fatigue, endurance, spasticity and numbness over the 12-month trial using BVT. Of even more importance were that these symptomatic improvements carried over into improved ADLs. Statistically significant improvements were seen in walking, stair climbing, car transfers, bed transfers, toilet transfers, bathtub transfers, and bed positioning. The Karnofsky Performance Scale results improved from an initial score of 50 to 65, indicating that the people with MS in this study progressed from needing a considerable amount of self-care to needing a minimal amount. With more than 68 percent of patients enrolled in the study experiencing some kind of positive effects from the venom, it is clear that BVT is a promising therapeutic avenue for researchers of MS to pursue. Further research needs to be done with tighter controls on data

collection before wholeheartedly embracing BVT as an answer for patients with MS. It is also clear that further study of the venom itself should be performed in order to determine the mechanism of action of the venom on MS, as this would lead to further research and therapeutic options.

L39 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2001 ACS
2000:191197 Document No. 132:232740 Protein and cDNA sequences of honey **bee venom** protein PX3.101, and uses thereof in the treatment of various diseases. Cui, Xiangmin; Lu, Yuefeng (Pan Pacific Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2000015774 A1 20000323, 80 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US21077 19990913. PRIORITY: US 1998-100172 19980914.

AB The invention provides protein and cDNA sequences of a novel protein, PX3.101, which can be isolated from honey **bee venom**. The invention also provides pharmaceutical compns. based upon PX3.101 polypeptide and methods for using same in the treatment of various diseases, including various inflammatory diseases such as rheumatoid arthritis. The invention further relates to the treatment of diseases assocd. with chemokine (esp. IL-8) imbalances, wherein PX3.101 inhibits the binding of a chemokine with its receptor.

L39 ANSWER 4 OF 12 MEDLINE DUPLICATE 1
2001041373 Document Number: 20529243. PubMed ID: 11074395. Treatments for fatigue in **multiple sclerosis**: a rapid and systematic review. Branas P; Jordan R; Fry-Smith A; Burls A; Hyde C. (West Midlands Development and Evaluation Service, The University of Birmingham, Birmingham, UK.) HEALTH TECHNOLOGY ASSESSMENT, (2000) 4 (27) 1-61. Ref: 80. Journal code: CUT. ISSN: 1366-5278. Pub. country: ENGLAND: United Kingdom. Language: English.

AB BACKGROUND: **Multiple sclerosis** (MS) is an important problem both for people with the disease and for society. There is no cure, and alleviation of symptoms forms the cornerstone of care. Excessive fatigue that severely limits activity is experienced by at least two-thirds of the estimated 60,000 people with MS in the UK. OBJECTIVES: (1) To identify current treatments for fatigue in MS and their evidence-base. (2) To systematically review the evidence for those treatments that have been investigated in more than one rigorous study, in order to determine their effectiveness and cost-effectiveness. METHODS: The review was carried out in two stages: a formal scoping review (to assess the range of interventions used by people with MS), and a systematic review for treatments that had been identified as promising and that had been investigated in clinical trials (as identified in the scoping review). A systematic review of research on costs and cost-effectiveness of those interventions identified as promising was also performed. Electronic databases, including MEDLINE and EMBASE, were searched for the period 1991-June 1999 (scoping review) and 1966-December 1999 (systematic review). Reference lists from publications were also searched, and experts were contacted for any additional information not already identified. RESULTS: Interventions identified for the treatment of

fatigue in MS (1) Behavioural advice. This is the main element of initial clinical management and no rigorous research of its effectiveness was identified. (2) Drugs (amantadine, pemoline, potassium-channel blockers and antidepressants). (3) Training, rehabilitation and devices (cooling vests and electromagnetic fields). (4) Alternative therapies (**bee venom**, cannabis, acupuncture/acupressure and yoga). Only two drugs, amantadine and pemoline, met the criteria for full systematic review. RESULTS - EFFECTIVENESS OF AMANTADINE: One parallel and three crossover trials were found, involving a total of 236 people with MS. All studies were open to bias. All studies showed a pattern in favour of amantadine compared with placebo, but there is considerable uncertainty about the validity and clinical significance of this finding. This pattern of benefit was considerably undermined when different assumptions were used in the sensitivity analysis. RESULTS - EFFECTIVENESS OF PEMOLINE: One parallel and one crossover trial were found involving a total of 126 people with MS. Both studies were open to bias. There was no overall tendency in favour of pemoline over placebo and an excess of reports of adverse effects with pemoline. RESULTS - HEALTH ECONOMIC ANALYSIS: The drug costs of amantadine and pemoline are modest (pound 200 and pound 80 per annum, respectively). No economic evaluations were identified in the systematic review, and available data were insufficient to allow modelling of cost-effectiveness in this rapid review. CONCLUSIONS: There is insufficient evidence to allow people with MS, clinicians or policy makers to make informed decisions on the appropriate use of the many treatments on offer. Only amantadine appears to have some proven ability to alleviate the fatigue in MS, though only a proportion of users will obtain benefit and then only some of these patients will benefit sufficiently to take the drug in the long term. CONCLUSIONS - RECOMMENDATIONS FOR RESEARCH: The frequency, severity and impact of fatigue, the poverty of available research, and the absence of any ongoing research, suggest that new research is an urgent priority. People with MS, clinicians and policy makers should work together to ensure that the evidence required is collected as quickly as possible by encouraging involvement in rigorous research. Research should not be restricted to the two drugs reviewed in depth in this report. All interventions identified in the scoping review (see above) should be considered, as should basic scientific research into the underlying mechanism of fatigue in MS.

L39 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2001 ACS

1998:126370 Document No. 128:189186 Delivery of tolerogenic antigens via edible plants or plant-derived products. Welter, Lisa M. (Agrivax Incorporated, USA; Welter, Lisa M.). PCT Int. Appl. WO 9806861 A2 19980219, 47 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US13634 19970805. PRIORITY: US 1996-23973 19960815.

AB Autoantigens and allergens can be expressed in transgenic plants, and the plants, or products derived therefrom, used as foods or beverages to prevent or treat autoimmune diseases or allergic reactions. Thus, expression cassettes were constructed for the following transgenic plant systems: (1) human myelin basic protein expression in potato; (2) human type II collagen in corn; and (3) S-antigen and/or interphotoreceptor retinoid-binding protein IRBP in soybean and sunflower. Feeding transgenic potato contg. myelin basic protein was effective in mice with relapsing-remitting exptl. autoimmune encephalitis.

L39 ANSWER 6 OF 12 MEDLINE

1998411619 Document Number: 98411619. PubMed ID: 9739302. A therapeutic bee sting?. Cerrato P L. RN, (1998 Aug) 61 (8) 57-8. Ref: 5. Journal code: TWP; 20010080R. ISSN: 0033-7021. Pub. country: United States. Language: English.

L39 ANSWER 7 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
1997:431249 Document No.: PREV199799730452. Apitherapy in the rehabilitation of patients with **multiple sclerosis**.
Krivopalov-Moscvin, I. International Centre Med., Chelyabinsk Russia. Journal of the Neurological Sciences, (1997) Vol. 150, No. SUPPL., pp. S264. Meeting Info.: XVI World Congress of Neurology Buenos Aires, Argentina September 14-19, 1997 ISSN: 0022-510X. Language: English.

L39 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2001 ACS
1996:756546 Document No. 126:17804 Human antibodies derived from immunized xenomice. Kucherlapati, Raju; Jakobovits, Aya; Klapholz, Sue; Brenner, Daniel G.; Capon, Daniel J. (Cell Genesys, Inc., USA). PCT Int. Appl. WO 9634096 A1 19961031, 64 pp. DESIGNATED STATES: W: AU, CA, FI, HU, JP, KR, NO, NZ; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US5500 19950428.
AB Antibodies with fully human variable regions against a specific antigen can be prepd. by administering the antigen to a transgenic animal which has been modified to produce such antibodies in response to antigenic challenge, but whose endogenous loci have been disabled. Various subsequent manipulations can be performed to obtain either antibodies per se or analogs thereof.

L39 ANSWER 9 OF 12 SCISEARCH COPYRIGHT 2001 ISI (R)
93:135109 The Genuine Article (R) Number: KP439. **BEE VENOM** THERAPY FOR **MULTIPLE-SCLEROSIS**. MRAZ C (Reprint).
AMERICAN BEE JOURNAL (MAR 1993) Vol. 133, No. 3, pp. 192. ISSN: 0002-7626.
Language: ENGLISH.

L39 ANSWER 10 OF 12 MEDLINE
86312094 Document Number: 86312094. PubMed ID: 3462567. **Bee venom** and chronic inflammatory disease. Fisher R B. NEW ZEALAND MEDICAL JOURNAL, (1986 Aug 27) 99 (808) 639. Journal code: OBQ; 0401067. ISSN: 0028-8446. Pub. country: New Zealand. Language: English.

L39 ANSWER 11 OF 12 MEDLINE DUPLICATE 2
84191807 Document Number: 84191807. PubMed ID: 6717729. Erythrocyte membrane glycerophospholipid organization is normal in **multiple sclerosis**. Hunter M I; Lao M S; Davidson D L. NEUROCHEMICAL RESEARCH, (1984 Jan) 9 (1) 103-8. Journal code: NX9; 7613461. ISSN: 0364-3190. Pub. country: United States. Language: English.
AB The phospholipid composition of erythrocyte membranes from patients with **multiple sclerosis** (MS) was found to be normal, in agreement with previous reports. The transbilayer asymmetry of the glycerophospholipids in MS red cells was probed using **bee venom** phospholipase A2 and was also found not to be significantly different from normal. Abnormal membrane glycerophospholipid organisation is therefore not involved in the increased red cell size, osmotic fragility, and electrophoretic mobility associated with MS.

L39 ANSWER 12 OF 12 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 3
78191901 EMBASE Document No.: 1978191901. Peripheral nerve changes induced by
local application of **bee venom**. Saida K.; Mendell J.R.; Sahenk Z.. Div. Neurol., Dept. Med., Ohio State Univ., Columbus, Ohio, United States. Journal of Neuropathology and Experimental Neurology 36/5 (783-796) 1977.
CODEN: JNENAD. Pub. Country: United States. Language: English.

AB In an attempt to elucidate the pathogenesis of neurologic complications of hymenoptera stings a series of experiments were performed in rats and rabbits. The local application of honey **bee venom** to the sciatic nerve produced a spectrum of changes. At the site of venom injection severe Wallerian degeneration was seen. In addition there were focal areas of dissolution of the myelin sheaths also affecting the cytoplasm, plasma membrane and basement membrane of the Schwann cells. This change was similar to the 'smudged appearance' of myelin in tissue culture following incubation with sera from animals with EAE and patients with **multiple sclerosis**. The myelin sheaths proximal to the site of honey **bee venom** injection were separated into a honey-combed type pattern. Depending upon the plane of section these areas were composed of parallel and bisecting linear membranes and circular profiles arranged in a hexagonal array. This change was identical to that observed with the application of snake venom phospholipase A and lysophosphatidyl choline and resembled the vesicular disruption observed in myelin sheaths in experimental demyelinating conditions. In rabbits and rats immunized with **bee venom** no cross reacting antibodies to peripheral nerve myelin were seen. No evidence of delayed hypersensitivity to myelin was seen in Lewis rats following injection of peripheral nerves with honey **bee venom**. These studies indicate that high concentrations of **bee venom** in close proximity to peripheral nerves could produce local changes in the nerve leading to a mononeuropathy. The pathogenesis of the diffuse CNS and PNS demyelinating conditions remains to be elucidated.

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L41 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2001 ACS
2000:191197 Document No. 132:232740 Protein and cDNA sequences of honey **bee venom** protein PX3.101, and uses thereof in the treatment of various diseases. Cui, Xiangmin; Lu, Yuefeng (Pan Pacific Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2000015774 A1 20000323, 80 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US21077 19990913. PRIORITY: US 1998-100172 19980914.

AB The invention provides protein and cDNA sequences of a novel protein, PX3.101, which can be isolated from honey **bee venom**. The invention also provides pharmaceutical compns. based upon PX3.101 polypeptide and methods for using same in the treatment of various diseases, including various inflammatory diseases such as rheumatoid arthritis. The invention further relates to the treatment of diseases assocd. with chemokine (esp. IL-8) imbalances, wherein PX3.101 inhibits

the binding of a chemokine with its receptor.

L41 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2001 ACS
1996:756546 Document No. 126:17804 Human antibodies derived from immunized xenomice. Kucherlapati, Raju; Jakobovits, Aya; Klapholz, Sue; Brenner, Daniel G.; Capon, Daniel J. (Cell Genesys, Inc., USA). PCT Int. Appl. WO 9634096 A1 19961031, 64 pp. DESIGNATED STATES: W: AU, CA, FI, HU, JP, KR, NO, NZ; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US5500 19950428.
AB Antibodies with fully human variable regions against a specific antigen can be prepd. by administering the antigen to a transgenic animal which has been modified to produce such antibodies in response to antigenic challenge, but whose endogenous loci have been disabled. Various subsequent manipulations can be performed to obtain either antibodies per se or analogs thereof.

L41 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2001 ACS
1996:577842 Document No. 125:219609 Chemically-defined non-polymeric valency
platform molecules and conjugates thereof. Coutts, Stephen M.; Jones, David S.; Livingston, Douglas A.; Yu, Lin (La Jolla Pharmaceutical Company, USA). U.S. US 5552391 A 19960903, 59 pp. Cont.-in-part of U.S. 5,276,013. (English). CODEN: USXXAM. APPLICATION: US 1993-152506 19931115. PRIORITY: US 1990-466138 19900116; US 1990-494118 19900313; US 1991-652648 19910208; US 1992-914869 19920715; US 1993-118055 19930908.
AB Chem.-defined, non-polymeric valency platform mols. and conjugates comprising chem.-defined valency platform mols. and biol. or chem. mols. including polynucleotide duplexes of at least 20 base pairs that have significant binding activity for human **lupus** anti-dsDNA autoantibodies. The polynucleotide duplex-contg. conjugates are useful as
toleragen for treating human autoimmune disease or systemic **lupus** erythematosus. In example, chem.-defined valency platform mols. were synthesized, conjugated with polynucleotide (PN) and hemagglutinin or sheep red blood cell, and used as toleragen to reduce PN-specific antibody-producing cells. Similarly, conjugates of the platform mols. and
melittin peptides were prepd. for tolerizing mice to melittin.

L41 ANSWER 4 OF 4 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
80248728 EMBASE Document No.: 1980248728. Conglutinin in the study of immune complexes. Macanovic M.; Lachmann P.J.. Inst. Nephrol., 71000 Sarajevo, Yugoslavia. FOLIA MED. FAC. MED. UNIV. SARAVIENSIS 14/1 (41-49) 1979. CODEN: FMFUAM. Pub. Country: Yugoslavia. Language: English. Summary Language: French; Russian.
AB A simple assay for the detection of circulating immune complexes was developed using 125I-labelled conglutinin and subsequent precipitation of conglutinin bound complexes with polyethylene glycol. The test was applied
to the sera of patients (systemic **lupus** erythematodes, Burkitt's lymphoma) and to immune complexes at various dilutions of ovalbumin / antiovalbumin, aggregated human IgG, and **bee venom** / anti **bee venom**. The sensitivity of the test is up to 8 .mu.g/ml of complexes. Conglutinin was also used to fractionate the antibody component of immune complexes; pepsin digested antibody was isolated as F(ab')2 and further tested with corresponding antigen.

=> s kim c?/au

L42 25914 KIM C?/AU

=> s l42 and bee venom

L43 3 L42 AND BEE VENOM

=> dup remove l43

PROCESSING COMPLETED FOR L43
L44 3 DUP REMOVE L43 (0 DUPLICATES REMOVED)

=> d l44 1-3 cbib abs

L44 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2001 BIOSIS
1994:190290 Document No.: PREV199497203290. Apitoxin (**bee venom**) therapy for chronic pain. **Kim, Chistopher M.**. Monmouth Pain Inst. Inc., Red Bank, NJ 07701 USA. Acupuncture & Electro-Therapeutics Research, (1993) Vol. 18, No. 3-4, pp. 264-265. Meeting Info.: 9th International Symposium on Acupuncture and Electro-Therapeutics New York, New York, USA October 14-17, 1993 ISSN: 0360-1293. Language: English.

L44 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2001 BIOSIS
1989:429996 Document No.: BA88:88254. **BEE VENOM** THERAPY FOR ARTHRITIS. **KIM C M**. MONMOUTH PAIN INST. INC., RED BANK, N.J., U.S.A. 07701.. RHUMATOLOGIE, (1989) 41 (3), 67-72. CODEN: RHUMAY. Language: English.
AB **Bee Venom** therapy for arthritis remains somewhat controversial. Unfortunately, there are very few controlled studies available to guide clinical practice. One Hundred and Eight patients with longstanding history of arthritis (RA or OA) who failed to respond to conventional medical treatment were used as subjects (Sept. 85 to Sept. 87). Participation was on a voluntary basis as denoted by informed consents from all subjects. All subjects were tested for possible allergic reaction before initial treatment. 0.1 ml. standard BV-10 was injected intradermally twice a week. The number of injections increased gradually each subsequent treatment until evaluation showed markedly improved or completely resolved. Pain was most common problem with subjects. Pain measure included the McGill Pain Questionnaire and Visual Analog Scales. Clinical evaluation included serial physical examinations and the thermographic findings. Each subject was followed 6 months to 2 years after finished treatment. Most of subjects, showed slight improvements after 3rd session and marked improvement average 12th treatment. Total 33,644 injections were given. No clinical complications or serious side effects were observed in any subjects who participated in the study. It was concluded the **bee venom** therapy is safe, effective and has no serious side effects, as long as a person is not allergic to **bee venom**. The preliminary results highly suggest that **bee venom** therapy is a new alternative approach for arthritis victims who failed to respond to the conventional medical treatments.

L44 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2001 BIOSIS
1987:391087 Document No.: BR33:71227. **BEE VENOM** THERAPY FOR ARTHRITIS AND NEURALGIAS. **KIM C M**. MONMOUTH PAIN INST., 46 ENGLISH PLAZA, RED BANK, N.J.. FIFTH WORLD CONGRESS ON PAIN, HAMBURG, WEST GERMANY, AUGUST 2-7, 1987. PAIN. (1987) 0 (SUPPL 4), S262. CODEN: PAINDB. ISSN: 0304-3959. Language: English.

=> s l3 and "about 0.1 mg and about 10.0 mg"

L45 0 L3 AND "ABOUT 0.1 MG AND ABOUT 10.0 MG"

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	240.42	240.57

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.00	-10.00

STN INTERNATIONAL LOGOFF AT 12:30:26 ON 05 DEC 2001